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ABSTRACT

This student text presents instructional materials for a unit of science within the Biomedical Interdisciplinary Curriculum Project (BICP), a two-year interdisciplinary precollege curriculum aimed at preparing high school students for entry into college and vocational programs leading to a career in the health field. Lessons concentrate on the circulatory system, with emphasis on the heart and blood vessels, blood and its properties, and the urinary tract. Reading materials, graphs, illustrations, and problems accompany each of 23 sections. (CS)

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BIOMEDICAL SCIENCE

UNIT III

THE CIRCULATORY SYSTEM IN HEALTH AND SCIENCE

THE HEART AND BLOOD VESSELS;
BLOOD AND ITS PROPERTIES;
THE URINARY TRACT

STUDENT TEXT

REVISED VERSION, 1976

THE BIOMEDICAL INTERDISCIPLINARY CURRICULUM PROJECT

SUPPORTED BY THE NATIONAL SCIENCE FOUNDATION

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SECTION 1: INTRODUCTION TO THE CIRCULATORY SYSTEM

1-1 The Circulation Unit

As you have probably realized by now, none of your body systems functions independently. All of your systems work together to form a living, functioning individual. At some point in the discussion of each body system it becomes necessary to bring in its role in relation to other systems.

The topic of this unit is the circulatory system, which is the system responsible for the movement of blood throughout the body. The subject should be a familiar one, for it has come up a number of times in earlier units. For example, in the Respiration Unit we discussed the role of the blood in transporting oxygen from the lungs to the cells, and carbon dioxide in the opposite direction. In the Nutrition Unit we saw that nutrients we obtain from food are carried by the blood to where they are needed. We also saw that the hormones which regulate many of our body systems travel through the bloodstream to their destinations.

Thus you should already be aware of the principal function of the circulatory system. It is to transport nutrients and other substances to where they are needed and to carry waste materials to where they may be eliminated from the body.

This unit consists of three major sequences. The first sequence is devoted to the heart (the pump that drives the system) and the blood vessels. In this sequence you will have an opportunity to learn about and perform several of the tests used in the diagnosis of heart disease and disease of the blood vessels.

The second sequence of the unit focuses on the blood itself--its composition and its several important functions. Here you will be performing some of the tests used in the clinical analysis of blood samples.

The third major portion of the unit is concerned with the kidneys. Although these organs are usually classed as part of a separate system of their own, the kidneys play a role that is closely related to that of the circulatory system. Near the end of this sequence, you will have a chance to design and construct a model artificial kidney that operates on the same principles as the artificial kidneys used in modern hospitals.

Medically, the circulatory system is of prime importance. Heart disease alone is the cause of as many deaths in American men as all other causes combined. And for American women, diseases of the heart and blood vessels cause as many deaths as all other causes combined. Many other diseases, not directly related to the circulatory system, cause changes in the blood and are detected by various blood tests, some of which you will be performing.

The kidneys, too, are of great medical interest. For example, they are the only organs thus far to be successfully transplanted almost routinely. The product of the kidneys--urine--often provides clues for the diagnosis of disease.

This unit will help you to understand why the circulatory system is important, how it works, and what happens when the system or one of its parts does not function properly.

1-2 Sir William Harvey and His Theory of Circulation

Where does our blood go?

Sir William Harvey was the doctor to King James I of England (for whom the King James Bible is named). In 1628, Harvey published a theory that contradicted almost all medical authorities of the time. Since the days of the Ancient Greeks, it had been believed that the blood moved in a "back-and-forth" fashion in the vessels. They thought that the heart somehow pushed blood out into the vessels and then sucked it back again.

Harvey, however, took a closer look. As a result of a number of experiments, he was able to demonstrate two things. First, he observed that the heart pumps blood into one set of vessels, called arteries. The arteries always carry blood away from the heart. He also found that a different set of vessels, called veins, always carry blood to the heart.

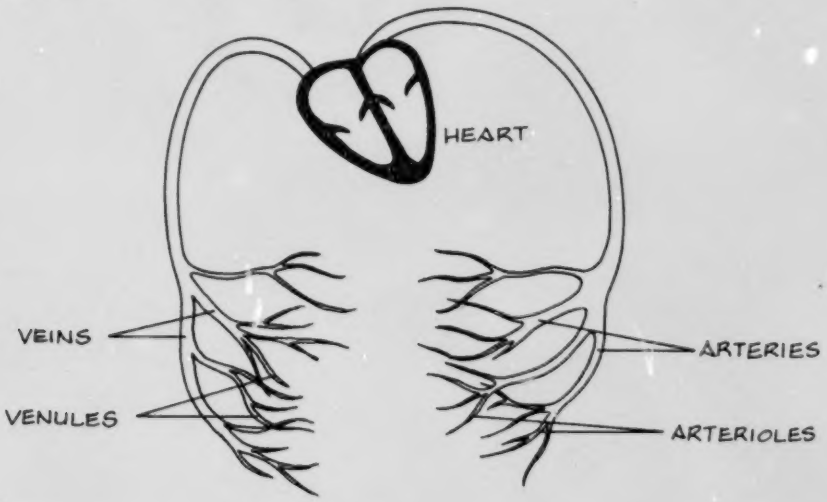
But was it the same blood flowing into the arteries that entered the heart from the veins? Harvey made some rough calculations. He figured that the heart pumps out

more blood in a half-hour than is contained in the entire body. (Actually, this much blood is pumped by the heart in closer to one minute, but Harvey was right in principle.

There appeared to be only one way to make sense of these observations. Harvey concluded that it was the same blood being pumped out and returned to the heart, over and over again. In other words, blood "circulates" (which comes from the word for "circle").

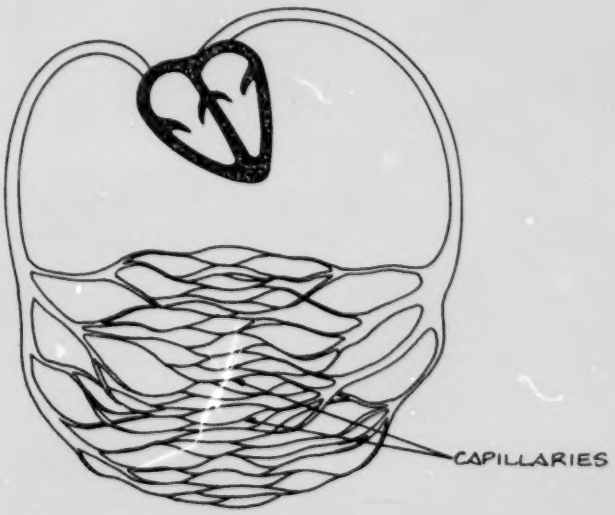
The scientists of Harvey's day remained unconvinced, because no one had been able to find vessels connecting arteries and veins. Instead they observed that the arteries branch into smaller and smaller arteries (called arterioles) which eventually come to an end. And the same was true for the veins, which branched into smaller and smaller vessels called venules. (See Figure 1.)

FIG. 1



The problem was that Harvey and his contemporaries lacked the microscope, which was just being developed at that time. In 1661--just four years after Harvey's death--the Italian physician Marcello Malpighi found the connection between the arterioles and the venules. Using a primitive microscope to examine the lung tissue of frogs, Malpighi found that the arterioles and venules continue to branch into vessels that are too small to be seen with the naked eye. And connecting them were even thinner vessels (Figure 3). These connecting vessels are called capillaries (meaning "hair-like").

FIG. 2



Thus Harvey's theory proved to be correct. The circulatory system is continuous, and it recycles the same blood over and over again.

Why is the circulatory system of medical concern?

What are the five kinds of blood vessels?

Name three functions of blood.

What was Harvey's theory about blood circulation?

Vocabulary:

arteriole (ahr-TEER-ee-ole)--the smallest arteries.

artery (AHR-tur-ee)--a vessel carrying blood away from the heart.

capillary (KAP-ih-LAIR-ee)--minute blood vessel connecting arterioles with veins.

circulatory system--the organs, vessels, and fluids that are involved with the circulation of blood.

vein--a vessel carrying blood to the heart.

venule (VEN-yool)--the smallest veins.

SECTION 2: ARTERIES, VEINS AND CAPILLARIES

2-1 Your Blood Vessel "Tree"

How do the arteries, veins and capillaries differ in structure?

Have you ever seen tiny red branches in the whites of your eyes when they're bloodshot? These red branches are small blood vessels. Your arteries look like the branches of a tree because they branch into smaller arteries. After they enter an organ they keep on branching into smaller and smaller arteries. The smallest arteries are your arterioles. They're less than a millimeter in diameter.

Arterioles then branch into capillaries, our smallest vessels--only .006 mm in diamter. By comparison, the largest artery, the aorta, is 25 mm in diameter, about 3,000 times larger!

Blood from capillaries flows into venules, which are the smallest veins. These in turn connect up into fewer and fewer veins of a larger and larger size. The two largest veins empty directly into the heart.

The surface area taken up by the walls of all the capillaries is gigantic. Let's imagine the impossible and put all your capillary walls together into a single sheet. This sheet would be almost large enough to cover an officieal-sized football field: several thousand square meters. Yet capillary walls are so thin that if we folded up this huge sheet into a square a meter wide by a meter long, the whole folded-up sheet would be only about 1.5 millimeters thick. The capillary walls are so thin that nutriends are able to pass through them easily to get from your blood to your cells.

Let's consider arteries and veins in more detail. Like the lanes of a two-lane highway, an artery and a vein often lie right next to each other. Figure 1, on the following page, shows cross sections of a small artery and vein. The most noticeable difference is that the wall of the artery is thicker than the wall of the vein. The walls of both consist of three layers, but the center layer of muscle cells is much thicker in the artery than in the vein. The extra muscle cells in the walls of small arteries give them a strength that small veins do not have. Figure 1 shows the vessels as they look when blood is flowing through them. But during dissection it can be seen that the wall of a vein is flabby. This is not true of arteries.

The cavity that the blood flows through is lined with a slick layer. It lets blood move along easily. This layer is made of flat cells called endothelial cells. Capillary walls consist exclusively of these flat cells, which explains why their walls are so thin (Figure 1).

The blood pressure inside arteries and veins differs. If you cut a large artery, blood can shoot out into the air in a stream a few inches or more in length. That's

because the blood pressure in arteries is great. If you cut a vein, though, blood will only slowly dribble out. That's because as blood moves from arteries into arterioles and then through capillaries its pressure gets lower and lower. By the time blood gets into the veins, its pressure is only about a twentieth of what it was when it was in the arteries. This is why veins can get by with thinner walls than arteries. Arteries are adapted to carry blood at a higher pressure.

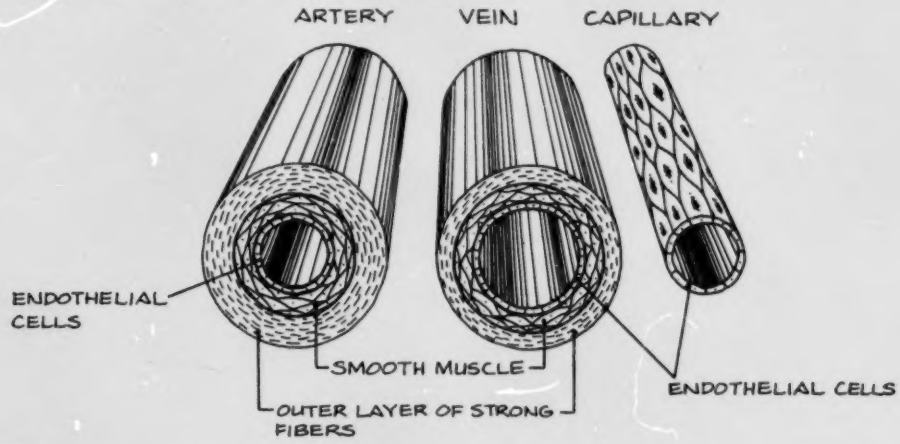


FIGURE 1: A small artery, a small vein, and a capillary. The artery and vein are magnified about 50X; the capillary about 1000X.

2-2 The Pressure and Flow of Blood

What keeps the blood moving through the circulatory system?

With each heartbeat about 70 ml of blood is squeezed into the aorta and the arteries that branch off from it. The walls of the arteries are elastic, and the force of the entering spurt of blood exerts enough pressure to stretch the arterial walls. When the heartbeat ends, the walls recoil and squeeze the blood farther along in the system. You feel this stretching of your arteries with each heartbeat whenever you take your pulse. The blood cannot be squeezed back into the heart because of a valve that snaps shut when the walls recoil.

The pressure of the blood entering the aorta is about 120 mm of mercury. (Recall from Unit I that atmospheric pressure is 760 mm Hg. All pressures discussed here are relative to--that is, above--atmospheric pressure.) From the aorta onward, the pressure of the blood drops all along the system until it is just slightly above zero where the blood re-enters the heart. This drop in pressure along the circulatory system is essential for the blood to circulate at all, for liquid will flow through a tube only if the pressure at one end is greater than the pressure at the other.

As the pressure of the blood changes, so does the speed with which it flows. But the pressure and speed change in different ways. The reason for the decrease in pressure is that part of the energy of the flowing blood is lost to friction, which in turn reduces the force exerted by the blood. The main factor controlling the speed of the blood, however, is the total cross-sectional area of the vessels through which it is flowing. And the situation is even more complicated than this. For example, the speed of the blood affects the amount of friction created and thus the pressure.

Instead of attempting to analyze how all these variables interact, we will move through the circulatory system step-by-step, paying attention mainly to the net effect. (See Figure 2, opposite.)

In the aorta and other large arteries the blood's pressure is about 120 mm Hg and its speed is about 40 cm/sec. By the time the blood reaches the smaller arteries the pressure has decreased only slightly, because these vessels are fairly wide and there are only slight frictional losses. At the same time, the speed decreases slightly because the blood is distributed over a somewhat larger total cross-sectional area.

When the blood moves into the arterioles, there are two important changes. These vessels are quite narrow, so that the friction increases greatly. In addition, the cross-sectional area of all the arterioles taken together is more than 100 times that of all the arteries. The net effect is to reduce the pressure to about 60 mm Hg and the speed to about 2 cm/sec.

As the blood enters the capillaries, the pathways are further narrowed, so that frictional losses remain high. But the most important change at the capillaries is the fact that the total cross-sectional area increases another hundredfold. The result is a pressure of about 20 mm Hg and a speed of only 0.05 cm/sec. The advantage of this "snail's pace" in the capillaries is that it allows ample time for the blood to release nutrients and pick up waste products from the cells of the body.

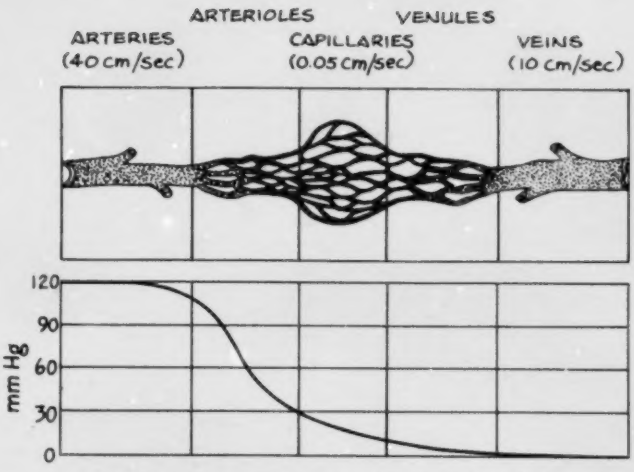


FIGURE 2: The speed and pressure of the blood as it circulates through the body.

After leaving the capillaries, the blood moves through progressively larger vessels (venules and veins) and the total cross-sectional area decreases step by step. As the area decreases, the blood picks up speed until it arrives at the heart with a speed of about 10 cm/sec. The small pressure remaining continues to decline. In the venules it is about 15 mm Hg and in the veins drops another 10 mm Hg, until it finally arrives at the heart with a pressure less than 5 mm Hg.

Notice how small the venous pressure is. It is not much pressure to accomplish the task of returning the blood to the heart. Consider, for example, that when you are standing up, the blood in your veins must be carried from your feet to your head against the force of gravity. Veins, like arteries, are elastic and they, too, tend to squeeze the blood along on its way. But your body has other mechanisms to keep blood flowing back to the heart, as well.

Many of your veins have special flaps, called valves, inside them. These valves permit the blood to move in only one direction, toward your heart (see Figure 3). When you move, your leg muscles press on the veins, which squeezes the blood inside them. Because of the valves, your muscles always squeeze the blood toward your heart.

If you remain motionless for a long time, the blood is not squeezed up as much and it tends to collect in your feet. Your feet may swell up. This may happen on long bus or airplane trips, making it difficult to get your shoes on, if you have removed them.

Sometimes valves become weak, seriously hampering the return of blood to the heart. As a result, blood collects in the veins, which may expand to four or five times their normal diameters. Eventually blue bulges form which can be seen standing out in the skin. These are called varicose veins. (Hemorrhoids are varicose veins in the recturm.)

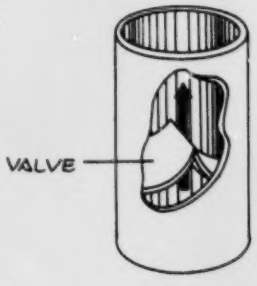


FIGURE 3: Leg vein cut to show a valve. The valve lets blood flow only toward the heart.

Your body has still one more mechanism which helps to return blood to your heart. Every time you inhale, your diaphragm descends and pushes on the large veins that pass through your abdomen, squeezing their blood toward your heart.

2-3 Changing the Distribution of the Blood

How is the flow of blood adjusted to meet different demands?

In Activity 1, you saw that your body has the capacity to adjust the amount of blood flowing to different organs. For example, when you run, more blood gets to where it's really needed, such as your leg muscles. How? The arterioles in those muscles widen. This lets more blood flow into those muscles. At the same time, less blood flows to organs you don't use for running, such as the digestive tract and kidneys. This happens because the arterioles in thos organs become narrower.

(Arterioles widen when the muscle cells inside their walls lengthen, and narrow when the muscle cells shorten.) This illustrates the importance of blood vessels in regulating flow.

Blood vessels change in other circumstances, too. Blushing results from the sudden widening of vessels in the facial skin, causing more blood to flow and thus change in color. A bump or swelling after a bruise is due in part to the widening of blood vessels, especially arterioles, in the area. This not only causes a color change, but the additional fluid in the extra blood entering the area causes swelling.

What are the main differences between arteries and veins? (Consider in particular the differences in structure, function, pressure and the presence or absence of valves.)

Describe the structure of capillary walls.

How does the stretching of arterial walls help propel blood through them?

What causes the pressure of blood to drop as it moves through the circulatory system?

Why does the blood speed up after it leaves the capillaries?

Why it is advantageous for the blood to move slowly in the capillaries?

What mechanisms does the body have for helping to return blood to the heart?

What causes varicose veins?

How is the amount of blood flowing to different organs controlled?

Vocabulary:

endothelial cells (EN-doh-THEE-lee-ul)--special flat cells which line the inner walls of blood vessels (and many other organs of the body). The walls of capillaries consist of a single layer of such cells.

varicose (VAIR-ih-kose)--enlarged.

SECTION 3: THE EXCHANGE OF FLUID AT THE CAPILLARIES

3-1 Blood Enters the Capillaries

How does fluid enter the bloodstream through the capillary walls?

Blood is a mixture of cells in a fluid. In one day, five gallons of liquid from your blood pass right through your capillary walls to leave the capillaries. That could leave you without any liquid in your blood! Fortunately while fluid leaves a capillary, fluid is also going back into it at places farther along the capillary. Capillaries have two ends, an arterial and a venous end (Figure 1).

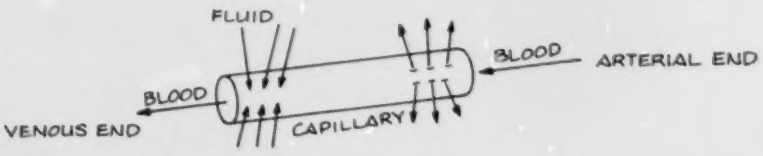


FIGURE 1: Blood flow through a capillary.

At the capillary's arterial end, the blood has a pressure of about 25 mm Hg. This pressure is what forces fluid out through tiny spaces in the wall. At the other end of the capillary the blood pressure is less, so not as much fluid is squeezed out. But what makes fluid go back into the capillary? To understand this, we first have to review diffusion through cell membranes.

3-2 Diffusion and Membranes

How does diffusion operate in the body?

The diffusion of a substance through a semipermeable partition separating one solution from another was illustrated in the Respiration Unit (p. 203). You may want to review the treatment of gas exchange between the alveoli and the pulmonary capillaries which provides an example of the significance of diffusion.

Diffusion is important to the body in other ways. It makes it possible for nutrients at high concentration in blood capillaries to be delivered to cells that are low or lacking in these nutrients. And this process is not limited to any particular cells.

All cells are surrounded by thin barriers known as cell membranes. Cell membranes are made up of intertwined lipid and protein. Figure 2 shows a group of cells, each bound by a distinct membrane.

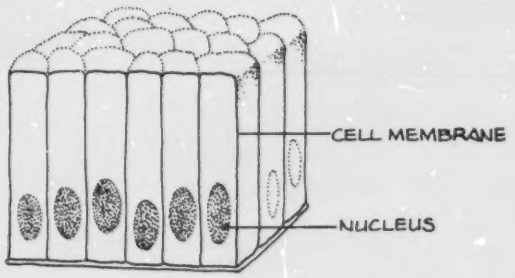


FIGURE 2: A group of skin cells.

Let us imagine a hypothetical cell surrounded by a solution of nutrients. We will also assume we can actually see the molecules of nutrients. We would be likely to see molecules entering and leaving the cell as in Figure 3. So the membrane is not an absolute barrier. We say that such a membrane is permeable--it permits molecules to enter and leave.

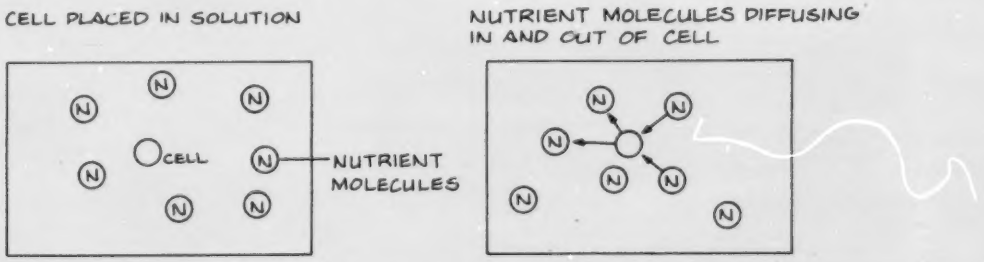


FIGURE 3: Diffusion in and out of cells.

There are three possible situations involving a cell in a fluid. See whether you can predict what would happen in each of these three situations before reading the answers.

(1) The fluid inside the cell and the fluid outside it have the same concentration of nutrients.

(2) The nutrient concentration is greater outside the cell than inside.

(3) The nutrient concentration is less outside the cell than inside.

In (1), nutrient molecules should enter and leave the cell at the same rate. In (2), the net movement of nutrient molecules should be into the cell. In (3), the net movement of nutrients should be out of the cell. From (3), we can see that the waste products like CO_2 that build up inside the cell can be removed from cells by diffusion.

Is it now possible to answer the question about what makes fluid enter a capillary? Almost! But we first have to explore one more concept.

3-3 Proteins and Diffusion

How do proteins surrounding a cell cause water to leave the cell?

Let's repeat the imaginary diffusion experiments above with a protein nutrient, because something special happens. Imagine that we place a cell in a solution that is 20 per cent protein. In general, proteins are too large to pass through the pores of a cell membrane. You might expect that nothing would move across the cell membrane in this case, but the actual result is that water molecules leave the cell. Why should this be?

Consider the concentration of water molecules on both sides of the membrane when the cell is placed in the protein solution (Figure 4A). Assume that the concentration of protein in this solution is greater than that of the fluid inside the cell. As a result, there is a higher concentration of water inside the cell than outside. So the water diffuses from the region of high concentration to the region of low concentration. The water flows out of the cell (Figure 4B). This flow of water is known as osmosis. The pressure generated during osmosis is known as osmotic pressure. By this definition, osmosis is actually a type of diffusion of fluids.

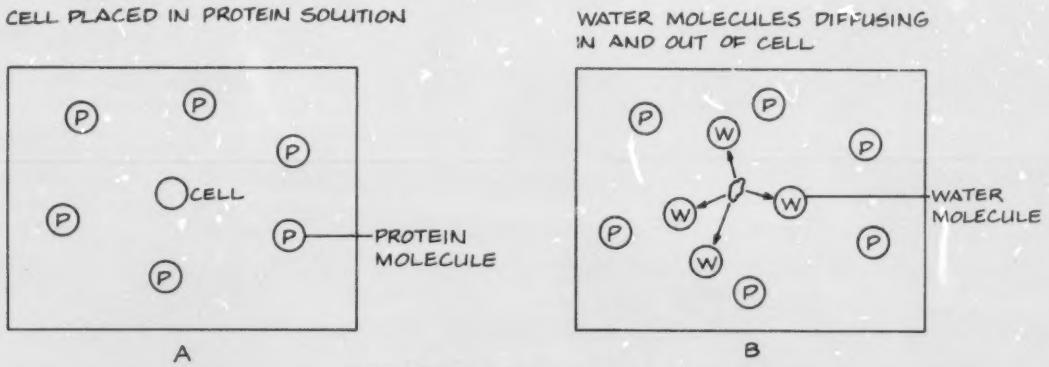


FIGURE 4: Osmosis.

An interesting thing happens when we take a cell like a red blood cell that is rich in protein and place it in distilled water. You tried this experiment in the Respiration Unit. Can you recall what happened? It's possible to guess the outcome without doing the experiment. Would the water concentration be greater inside or outside the cell? Clearly, the concentration must be greater outside since distilled water is 100 per cent water; inside the cell, the water is diluted by proteins and other substances. So we should predict that water would flow into the cell. In actual experiments, this can be shown to be true (Figure 5). The cell swells as water rushes in (Figure 5B) and will explode when the inside pressure gets high enough (Figure 5C).

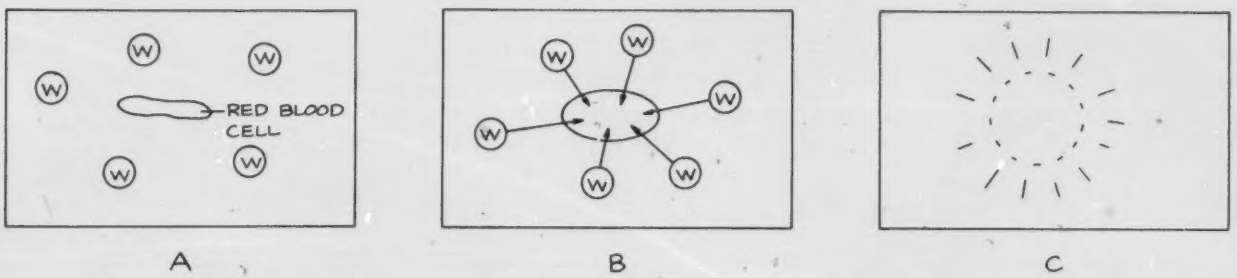


FIGURE 5: A. A red blood cell is placed in distilled water.
B. As water molecules rush in, the cell expands.
C. The internal pressure increases until the cell bursts.

3-4 Osmotic Pressure and Capillaries

What makes fluid go back into capillaries?

We will now return to this question because we have the background to answer it. The key principle was osmosis.

Consider Figure 6A (opposite). Fluid tends to diffuse out of a capillary because of the blood pressure inside the capillary. Recall that this pressure is greater at the arterial end than at the venous end. At which end would you expect more fluid to excape? (See Figure 6B.)

However, we must also consider the effect of osmotic pressure because the blood is much richer in proteins than the fluid that surrounds the blood vessels. Ignore blood pressure for a moment--how do the proetins in blood affect the movement of fluid into or out of the blood vessels? As you can see from Figure 6C, osmotic pressure causes fluid to re-enter the capillary.

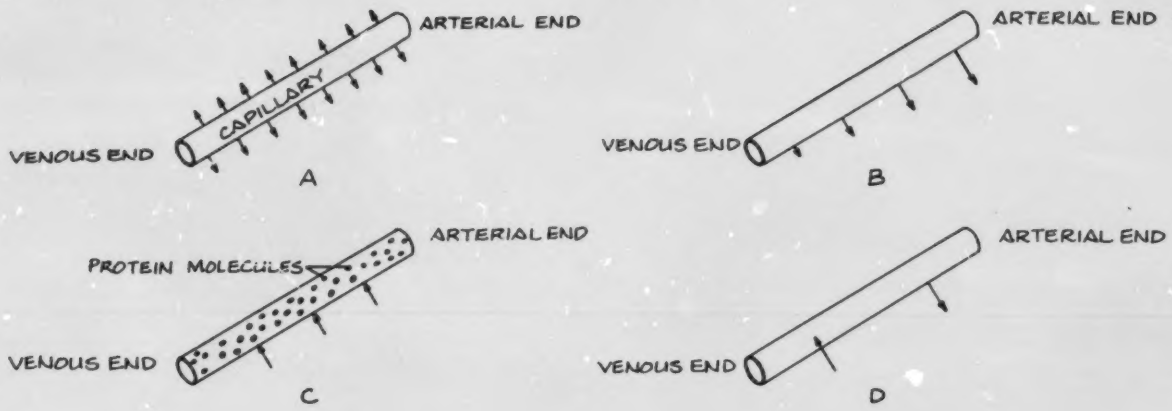


FIGURE 6: How blood pressure and osmotic pressure affect the movement of fluid into and out of a capillary.

A. Because of internal pressure, fluid tends to be forced out as shown by the arrows.

B. More fluid is forced out at the arterial end than at the venous end. This is indicated by the length of the arrows.

C. Because of protein molecules in blood, osmotic pressure forces fluid into the capillary.

D. The net effect is that fluid leaves the capillary at the arterial end and re-enters at the venous end.

So we have blood pressure forcing water out and osmotic pressure forcing the water back in. What is the net effect? Figure 6D shows that at the arterial end, the net effect is for fluid to move <u>out</u> of the capillary. This is because the blood pressure at the arterial end is greater than the osmotic pressure. However, the figure shows just the opposite occurring at the venous end. The blood pressure there is less than the osmotic pressure, so fluid <u>enters</u> the capillary at the venous end.

What will happen to a blood cell placed in distilled water? Why?

What are the chemical components of a cell membrane?

Describe the distinction between diffusion and osmosis.

What causes fluid to enter a capillary?

<u>Vocabulary</u>:

<u>cell membrane</u>--a lipid-protein envelope that surrounds a cell.

REVIEW SET 3:

In the following statements, certain words are underlined. If the statement is true, write "true" on a separate sheet of paper as you answer. If the statement is false, write the word or words which will replace the underlined word(s) to make the statement correct.

<u>EXAMPLE</u>: Emphysema is a disease of the <u>circulatory</u> system.

<u>ANSWER</u>: respiratory

1. The blood vessels with the thickest and most muscular walls are <u>veins</u>.

2. Capillary walls are <u>one</u> cell-layer thick.

3. Valves are found in arteries.

4. The movement of materials from regions of high concentration to low concentration is called diffusion.

5. The movement of blood in arteries is in spurts; the movement in veins is smooth and continuous.

6. The exchange of materials between the blood and the cells occurs across the walls of the arterioles.

7. The blood pressure in a capillary is higher at the arterial end than at the venous end.

8. Fluid flows out of the capillaries at the venous end and flows back in at the arterial end.

9. Blood pressure is higher in arteries than in veins.

10. Blood flow into the capillaries is supplied by the venules.

11. Cell membranes are composed of lipids and proteins.

SECTION 4: THE STRUCTURE OF THE HEART

4-1 The Right and Left Sides of the Heart

What is the heart like on the inside?

Much of your heart consists of a pair of ventricles. The term "ventricle" comes from the Latin word for "little belly," probably because early scientists thought a ventricle looked like one. The ventricles pump the blood out of the heart.

A few hundred years ago people knew a little about ventricles. A few scientists had even cut open dying animals to observe their hearts slowly beating to a stop. But there was one question even the most brilliant scholar in the 16th century could not answer: where did the blood pumped by each ventricle go?

The answer was found by a man we have already mentioned: William Harvey. After years of laboratory work he reported two key observations. The right ventricle pumps blood to the lungs. The left ventricle pumps blood to all the rest of the body.

Furthermore, each ventricle receives its blood from an atrium. "Atrium" is the Latin word for the entrance room of a house. The atria were named for entrance rooms because they are the entrance chambers through which blood enters the ventricles. When a ventricle is ready to be filled up with blood, there is a supply waiting in an atrium.

4-2 The Route Blood Travels Through the Heart and Lungs

How does the heart pump blood?

We have already stated (1) that the heart pushes blood through the body, and (2) that the left ventricle (Figure 1, opposite) has to push blood through all of your arteries except the ones in the lungs. This ventricle must exert a lot of pressure to force the blood through those vessels. The right ventricle, on the other hand, which pushes blood through arteries into the lungs, exerts only a fifth or a sixth as much pressure as the left one does. The left ventricle is adapted, by means of a thick muscular wall, to exert far more pressure than the right ventricle.

Now for a moment let's travel the route that blood always follows as it winds its way through the heart and lungs. Figure 2, opposite, shows the heart and lungs. Let's begin with the "used" blood coming into the heart from any vein except the ones from the lungs. This "used" blood empties into two huge veins called the venae cavae (Latin for "hollow veins"). The venae cavae lead into the right atrium.

From the right atrium blood travels to the right ventricle. When the ventricle is filled with blood, the heart beats. During the beat the right ventricle pushes

the blood into the pulmonary artery. The pulmonary artery branches into two arteries, which carry the blood to the two lungs.

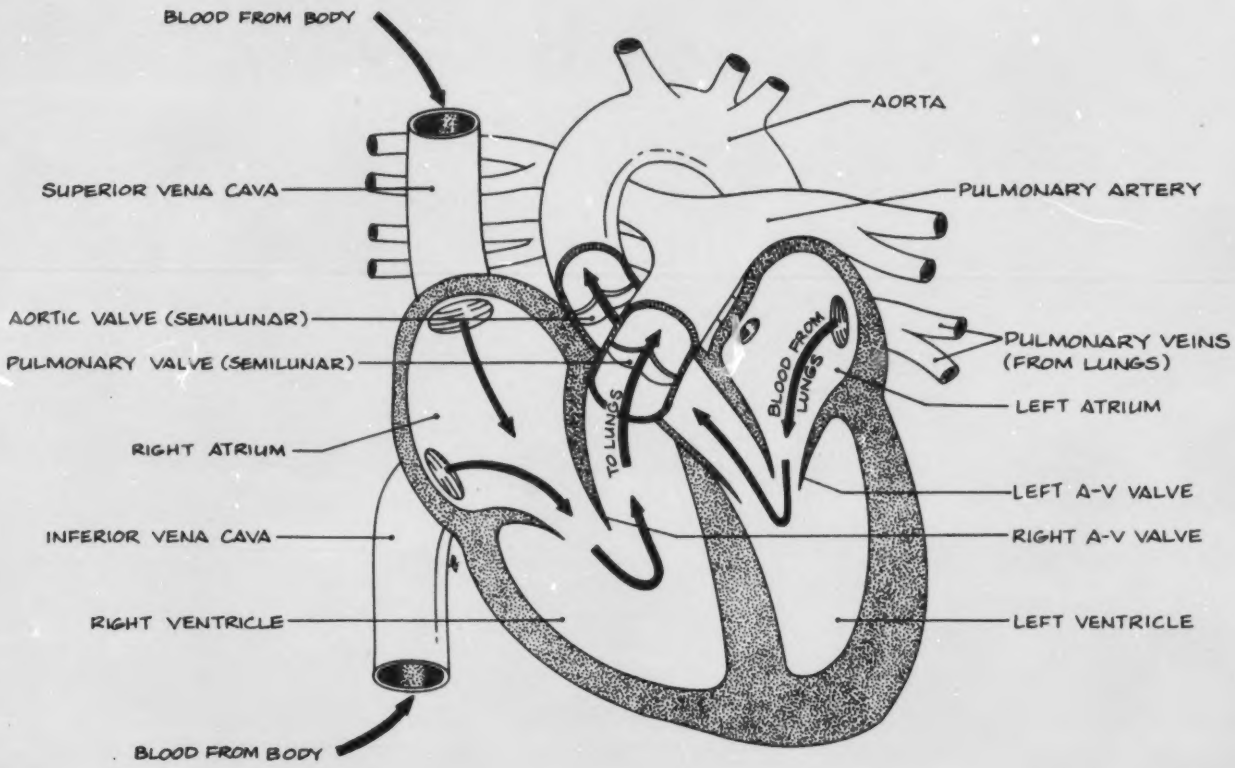


FIGURE 1: The human heart, drawn to make the inside visible. Arrows show the direction of blood flow.

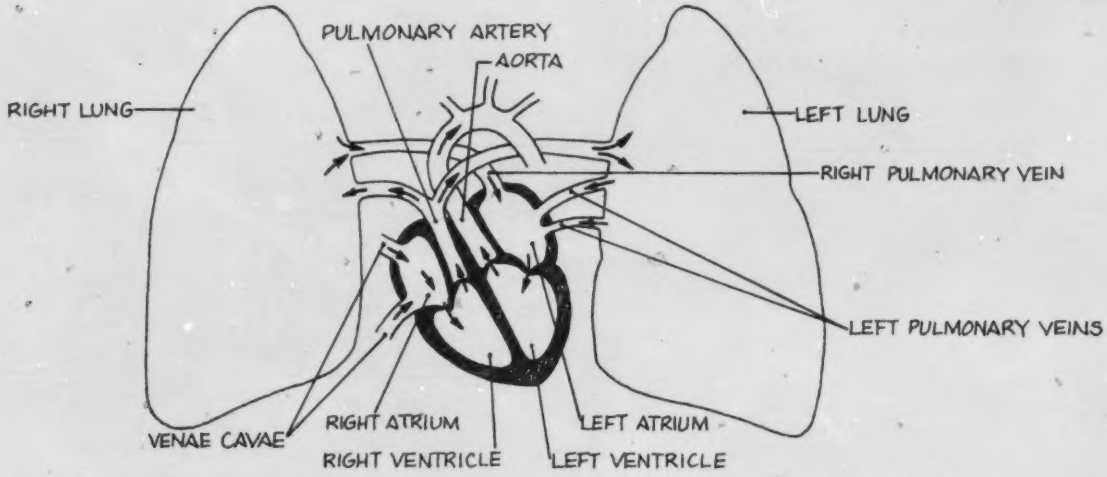


FIGURE 2: The path traveled by blood through the heart and lungs.

In the lungs, the blood picks up O_2 and CO_2. Oxygen-rich blood leaves the lungs in veins called pulmonary veins. These veins lead into the left atrium of the heart. (It is interesting to note that the veins in the lungs are the only veins in the body that carry oxygen-rich blood. Also the arteries in the lungs are unique in that they carry oxygen-poor blood.)

From the left atrium, blood goes into the left ventricle and fills it up. Then during the heartbeat, the left ventricle squeezes the blood into the aorta. The aorta branches into arteries that carry the blood everywhere except the lungs.

The right ventricle and the left ventricle both squeeze blood out at the same time during a heartbeat. As a result, blood from the right ventricle is being squeezed into the pulmonary artery at the same time that blood from the left ventricle is being squeezed into the aorta.

The tissues of the heart need their own supply of blood, too. The heart is supplied by two coronary arteries which branch off the aorta (see Figure 3). Coronary veins lie next to the coronary arteries. These veins empty directly into the right atrium.

A fluid-filled bag called the pericardium surrounds the heart. The fluid lubricates and protects the outside of the heart, enabling it to function smoothly.

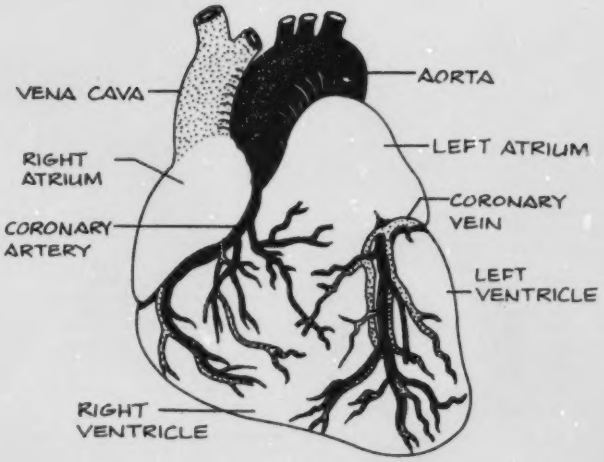


FIGURE 3: A coronary artery and vein.

4-3 Heart Valves in Health and Disease

Why are valves important?

Deep inside the heart are flaps of tissue. In an infant some of them are no larger than a dime, yet they are critical to life. They are valves.

In Section 2 we discussed the role of valves in returning venous blood to the heart. We also mentioned a valve at the junction of the heart and the aorta. The valves of the circulatory system are sets of flaps that act like one-way doors. They let blood through in one direction but not in the other. By doing this they insure that blood keeps moving forward, not backward. If some of it moved backward, the flow of blood would slow down or stop, which could endanger life.

There are four heart valves (Figure 4). Two of them are called atrioventricular, or "A-V" valves for short, because each lies between an atrium and a ventricle. These valves are very strong. They are attached to many cords made of strong fibers. When blood is flowing from the atria into the ventricles, the A-V valves are open. But when the ventricles squeeze blood out into the arteries, the A-V valves snap shut. This prevents blood from being forced backward into the atria.

The other pair of valves are called semilunar valves ("semi" means "half," and "lunar" means "moon"). When these valves are open their flaps resemble half-moons, as shown in Figure 4. The semilunar valves are open while the ventricles are pushing blood into the arteries. They close when the elastic walls of the arteries recoil, thus preventing blood from re-entering the ventricles. One of the semilunar valves, the aortic valve, prevents blood from flowing from the aorta into the left ventricle. The other semilunar valve, the pulmonary valve, prevents the flow of blood from the pulmonary artery into the right ventricle.

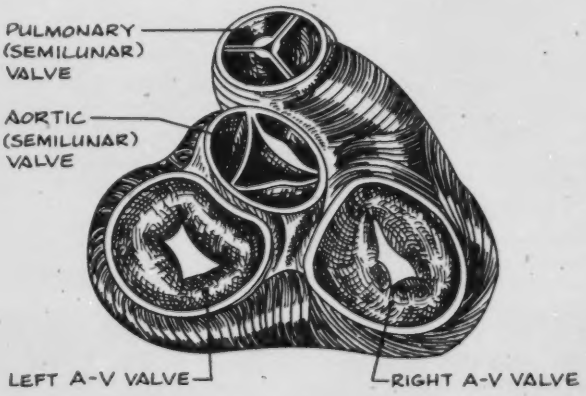


FIGURE 4: Top view of the heart, with the atria removed.

In a healthy heart, valves can open and close smoothly. But trouble may occur

when a heart valve is damaged by disease, such as in rheumatic heart disease, or is not fully formed at birth. Then, one of two things can happen. It may not close completely and so blood may leak backward. Or it may not open widely enough when it has to let blood through, and may slow down the flow of blood.

If either of these happens, the heart must work harder to pump blood. It may become overworked, and if the valve defect is serious enough, the heart may eventually fail. A doctor can tell whether a valve is defective by listening to the heart. Later we will see how artificial valves have been used to restore normal function of the heart.

Where does the right ventricle pump blood to? Where does the left ventricle pump blood to?

How is the left ventricle adapted to perform its function?

From which heart chamber does the left ventricle receive blood? From which does the right ventricle?

Are the venae cavae arteries or veins?

Is blood in the pulmonary veins high or low in oxygen?

Is blood in the pulmonary artery high or low in oxygen?

What is the general function of a heart valve?

Compare the function of valves in the circulatory and digestive systems.

What is the function of the coronary arteries?

Vocabulary:

aorta (a-OR-tuh)--the large artery which receives blood from the left ventricle of the heart.

atrioventricular valve (A-tree-oh-ven-TRIK-u-lar)--a valve which prevents blood from flowing from a ventricle into an atrium.

atrium (A-tree-um)--one of the two upper chambers of the heart, through which blood first enters the heart. Plural: atria (A-tree-uh).

pericardium (PAIR-ih-KAR-dee-uh)--a fluid-filled sac surrounding the heart.

pulmonary artery--the artery which receives blood pumped into it by the right ventricle and carries the blood to the lungs.

pulmonary veins--the veins that carry blood from the lungs to the left atrium.

semilunar valve (SEM-ee-LOO-nur)--a valve which prevents blood from flowing from an artery into a ventricle.

vena cava (VE-nuh KAY-vuh)--one of the two large veins which empty into the right atrium. Plural: venae cavae (VE-nee KAY-vee).

ventricle (VEN-trih-kul)--one of the two lower chambers of the heart, from which the blood is pumped into arteries.

SECTION 5: TESTING YOUR HEART

5-1 Measuring the Heart Rate

What are some of the measurements that can be made on the heart?

Because your heart is so vital, it is important to test whether it is functioning normally. There are a number of ways to test the heart. First is the heart rate, which is the number of heartbeats per minute.

Your heart rate is probably in the neighborhood of 70 beats per minute when you are relaxed. When you exercise hard it can go up to more than 200 beats per minute. In contrast, a resting elephant has a heart rate of only 25, and a mouse may have one of 500 or higher. (Usually the smaller an animal, the greater its heart rate.)

Since your arteries expand every time your heart beats, you can easily find your heart rate by placing a finger over an artery and taking your pulse. This kind of measure is called a pulse rate. It's the same as the heart rate.

In some situations, the pulse rate may decrease, such as during fear or severe grief. Many things increase your pulse rate:

1. Emotional state--when you're excited, angry or in pain.
2. Anticipating exercise, as well as exercise itself.
3. Fever.
4. Every time you inhale, your pulse rate goes up, and exhaling lowers it.
5. Suddenly standing up increases it. So does severe bleeding.

It's a good thing your pulse rate changes. For example, a faster pulse rate during exercise means more blood gets pumped to your muscles. Or, a faster pulse rate when you lose a lot of blood means the blood flow through vital organs is maintained.

Exercise and excitement not only raise your heart rate but also make your heart beat more strongly. That's why you can feel your heart pounding then.

There are a number of ways to find your heart rate, in addition to taking your pulse. Blood is hotter than your skin, so every time the heart pushes blood into skin vessels, the skin heats up. A skin temperature gauge can therefore be used to measure heart rate.

The amount of blood in your arterioles changes with each heartbeat. An electronic photocell can be used to measure the amount of light that passes through your fingertip. During each pulse in the arterioles, the amount of blood in them is temporarily increased, and your fingertip transmits less light. This arteriolar pulsing (and thus your heart rate) can be monitored with the BIP.

There is yet another way in which the heart rate can be monitored. The Greeks had a weapon called a "ballista," which hurled big rocks. (You've no doubt heard of "ballistic" missiles.) Your heart "hurls" your body very slightly every time it beats. If you sit still and cross one leg over the other and let it dangle, you may see a slight rhythmic movement of your foot. This is caused by blood suddenly moving in the arteries of your leg with each heartbeat.

How hard you're being thrown by your heart can be recorded with a technique called ballistocardiography. "Ballisto-" means "throwing," "cardio-" means "heart" and "graph" means a "record." So the term means a record of the heart throwing you. Here's how it works.

If you blow up a balloon and let it go, air gushes out of the opening at one end. The balloon shoots away from the gush. (See Figure 1A, opposite.) Rockets operate on the same principle.

The same thing happens to your heart (Figure 1B). When blood is pushed out in one direction, the heart and the rest of the body move in the opposite direction. A record of this movement can be made with special instruments.

5-2 Body Sounds

What causes the sounds of the heart?

Your body makes all kinds of sounds. Some you can make when you feel like it, such as yelling and talking and swallowing sounds.

Ever hear your stomach gurgle? It's a sound you don't have much control over. You don't have much control over your heartbeat, either. It's so quiet that you normally have to do special things to hear it.

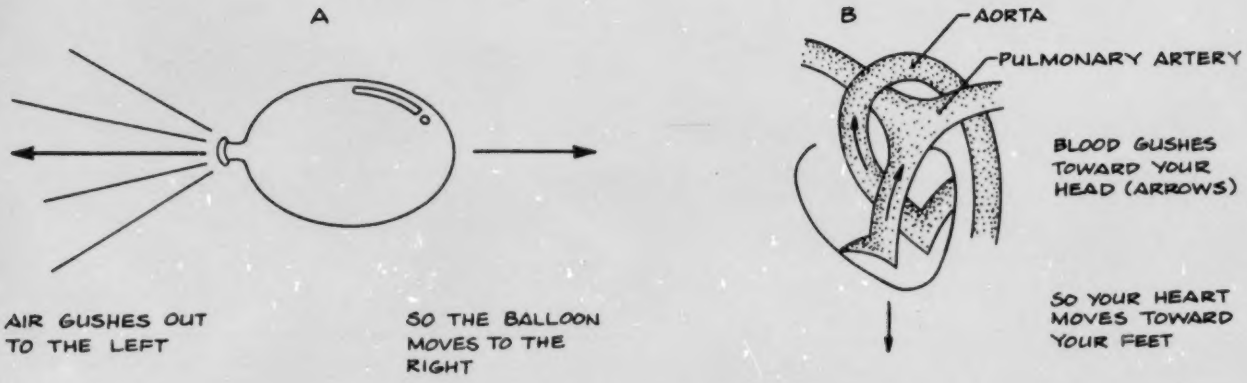


FIGURE 1: The principle of ballistocardiography.

Before René Laennec invented the stethoscope in 1819, doctors used to press their ears against their patients' chests to hear heart and breath sounds. This didn't always work too well, especially with obese people. Laennec found that when he listened through a paper or wooden tube he heard the sound better. That was the first stethoscope. ("Stetho-" means "chest" and "scope" means "spy" or "peer.") Modern instruments are made with two earpieces for better listening, and a bell or diaphragm to pick up more sound (see Figure 2).

Doctors use a stethoscope to listen to your heart, to the sound of air moving through your lungs, and to hear food being sloshed along through your digestive tract.

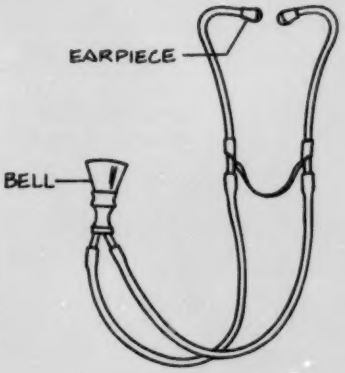


FIGURE 2: A stethoscope.

5-3 Why Does Each Heartbeat Make a Sound?

What is the role of valves in making heart sounds?

The only time liquids flowing in pipes make noise is when they bang against the walls of the pipes, as shown in Figure 3. Usually an obstruction makes them do this. That's what makes the heart sounds you hear in a stethoscope.

In the heart, the obstructions are closed valves. Valves open and close in rhythm with every heartbeat. When they open to let blood go forward, there is no sound. But when they close, and stop backflow, blood hits them and sounds are made.

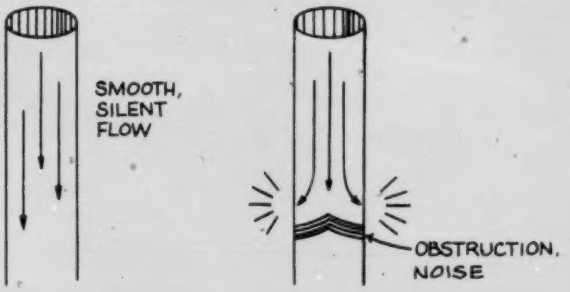


FIGURE 3: How an obstruction in a pipe leads to noise.

There are two main heart sounds, often described as "lub, dub." The first one ("lub") is made while the ventricles squeeze blood. This closes the A-V valves suddenly. When blood hits those closed valves, the sound is made, as in Figure 4 on the following page. The second sound ("dub") is made when the semilunar valves close and blood hits them. (See Figure 5 on the following page.) Some people have a third sound, too, made by blood hitting the ventricles as it runs in to fill between "dub" and the next "lub."

FIGURE 4: How blood hitting the closed A-V valves makes the first heart sound, "lub."

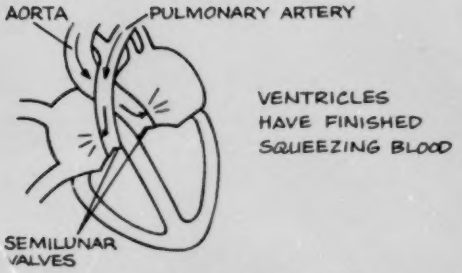


FIGURE 5: How blood hitting the closed semilunar valves makes the second heart sound, "dub."

Besides hitting a complete obstruction, there is another way in which blood can make noise. If a tube has a narrow place in it, this can make blood hit the walls and produce noise (Figure 6).

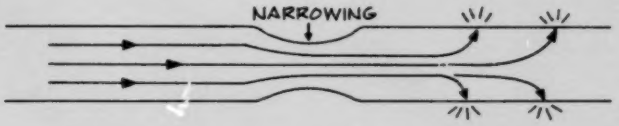


FIGURE 6: A narrowing in a tube can cause the liquid flowing in it to make a noise.

Some diseases partially block valves by making them narrower. Therefore when the valves are supposed to be fully open to let blood through, they are not--they are narrowed instead. This causes a sound to be made every time the ventricle squeezes blood through them. The sound of blood shooting through a narrow valve is one example of a murmur. A murmur is an abnormal heart sound. You need a stethoscope to hear one. Today, rheumatic fever is the main cause of narrow valves. A narrow valve is shown in Figure 7.

With a narrowed aortic valve, the heart has to squeeze harder to force the blood through it. This can overwork and eventually damage the heart. In such a case the valve can be sugically widened, or an artificial valve can be put in instead (Figure 8). Can you decide which way the artificial valve in Figure 8 would face in the aorta? (Hint: when the ball sits in the ring it seals it so no blood can get through. The ball can move around inside the cage.)

FIGURE 7: A. Normal open aortic valve.

B. Narrowed aortic valve. This aortic valve can't open all the way because its edges are stuck together by scars. This happens in rheumatic heart disease.

FIGURE 8: The artificial valve. A caged ball.

5-4 Sounds in Health and Disease

What does the physician or other health-care professional listen for through a stethoscope?

Your doctor listens for a lot of things in using the stethoscope on you. He or she may consider these questions.

1. Is the heart's rhythm steady?
2. Is the heart rate normal?
3. Are the heart sounds themselves normal? Are they too soft or too loud?

4. Are there any murmurs? If there are, it might mean a valve is diseased.

Not all the listening involves the heart and circulatory system.

Gurgles--Sometimes listening to your stomach with a stethoscope is helpful to the doctor. For example, in some inflammations, your stomach and intestines can stop making sounds all together. In stomach "flu," on the other hand, there are more sounds than normal.

Wheezes--People with asthma have narrower-than-normal bronchioles in their lungs during an attack. So, during breathing, the air that flows in and out whistles softly. Other kinds of diseases can cause crackling sounds or even reduced sounds if the air passages become filled with fluid. For example, if the heart becomes so weak that it can't pump blood out fast enough, blood can back up into the lungs. This happens when the coronary vessels become severely atherosclerotic. All that extra blood in the lungs can result in a disease process that causes delicate crackling sounds to be heard in the stethoscope. Recognizing these sounds helps in designing proper therapy.

What conditions increase the heart rate?

What is the importance to the body of a faster pulse rate during exercise? During severe blood loss?

Describe at least two ways to measure the heart rate.

What is a stethoscope? If you were marooned on a deserted island, how could you make one?

Name two conditions under which blood makes a sound.

How are the two main heart sounds made?

What is a murmur? What is the most common disease that causes a murmur? How does it do so?

What are some other abnormal sounds that may be detected with a stethoscope? What do they signify?

Vocabulary:

ballistocardiography (buh-LIST-o-KAR-dee-AH-gruh-fee)--the technique of recording the movement of the body caused by each heartbeat.

murmur--an abnormal heart sound. It often occurs when blood passes through an abnormal opening, such as a narrowed valve.

pulse rate--the number of expansions of an artery per minute. Each expansion is caused by blood being pumped into the artery by a heartbeat.

stethoscope (STETH-o-scope)--the device used to listen to body sounds.

SECTION 6: THE IMPORTANCE OF BLOOD PRESSURE

6-1 Case History: Male, Age 48

Mr. Samuels was 48 years old and always said that he'd never been sick a day. This day things were different. While walking to his office after lunch he felt a sharp pain in his chest, and a moment later he was lying on the street in pain and breathing heavily. With the help of an ambulance, 15 minutes later he was on an examining table in the emergency room of Central Hospital.

Three people stood over him. He saw a mask being held over his nose and mouth. Wires were attached to his body. The wires reminded him of the time he had had his heart checked during a physical exam.

"I've had a heart attack," he thought. The chest pain was still there.

"Pulse 140. Blood pressure 90 over 50," said the nurse. When the doctor heard these numbers he immediately ordered that a drug for Mr. Samuels' heart be injected into an arm vein. He also ordered a pain killer. Then the patient was placed in the Coronary Care Unit for close observation.

An hour later he received a visit from Dr. Gardner, the physician he had seen in the emergency room.

"You're a lucky man," said the doctor. "You've had a heart attack. But with proper care, we should have you out of here in a few weeks."

Mr. Samuels felt a bit more relieved now. He wondered what his blood pressure had to do with the heart attack. Why had his pressure dropped? What did it mean?

6-2 Low Blood Pressure

What causes a drop in blood pressure?

In this case history Mr. Samuels' blood pressure was dangerously low: 90 over 50. This means that his systolic blood pressure was 90 mm Hg and his diastolic blood pressure was 50 mm Hg. It is written 90/50.

Systolic blood pressure is the highest pressure exerted by the arterial blood during each heartbeat. It occurs during the time known as systole, when the ventricles contract to force blood into the arteries. Diastolic blood pressure is the lowest pressure that blood exerts in the arteries. It occurs at the time known as diastole, the time between heartbeats. In diastole, the ventricles are relaxed and are no longer pumping out blood.

For a man near 50 such as Mr. Samuels, the desirable systolic blood pressure is 125 ± 15 mm Hg and the desirable diastolic blood pressure is 75 ± 10 mm Hg. Mr. Samuels' pressure was below these values. At the same time, he had a high pulse rate--140 beats per minute. Both were a result of his heart attack. The attack damaged his heart so that it could not pump out blood as forcefully as before. The amount of blood entering his arteries with each heartbeat was less than normal, and this meant a lowered blood pressure. The heart responded by speeding up, but this didn't help at all. The reason for this is that when the heart rate is too high, there is not enough time between heartbeats for the ventricles to fill completely with blood. As a result, the ventricles pump less blood per heartbeat than normal.

In Mr. Samuels' case, the main function of therapy is to buy time--time for his heart damage to heal. His heart can never be as good as it once was, but if he survives the healing period, he may return to an almost-normal life.

As we have seen, the immediate cause of Mr. Samuels' low blood pressure was the fact that his heart was pumping less blood into his arteries than normal. Low blood pressure can also result from severe bleeding, for much the same reason. In this case, there is less blood to be pumped. In some conditions, there is a significant loss of water from the blood. This, too, reduces the total volume and hence the pressure of the blood.

Certain other conditions can cause the arterioles of the body to dilate (expand). In this case, the blood pressure drops because the walls of the vessels exert less force on the blood.

Thus there are two general ways in which low blood pressure can occur. One is a decrease in the volume of blood being circulated per unit time, either because of a faulty heart or because of an actual reduction in the total volume of blood in the system. The other is dilation of the arterioles. Either condition, if severe enough, can quickly lead to death because of an inadequate supply of oxygen to vital areas.

6-3 Hypertension

What causes blood pressure to increase?

As you might expect, hypertension (high blood pressure) results from just the opposite of the two factors that lead to low blood pressure. One cause is an increase in the volume of blood circulating. This happens when too much salt and water are retained in the body. The extra water increases the volume of the blood, which in turn raises the pressure. The kidneys play an important role in regulating the salt and water content of the blood, as we will consider in a later section.

Almost all cases of hypertension, however, are caused instead by an abnormal constriction or narrowing of the arterioles. The cause of this constriction is unknown in most cases. But, as was mentioned in the Nutrition Unit, there is considerable evidence that excessive intake of dietary sodium is somehow involved.

It is common for people's blood pressure to increase with age. But in many people the rise is so great that it endangers health. This is indicated by studies which show a correlation between high blood pressure and the risk of heart attack.

For a 15- to 20-year-old person, the desirable range for systolic blood pressure is 115 ± 15 mm Hg and 72.5 ± 12.5 mm Hg for diastolic blood pressure. As people get older the upper limits increase, so that for a 45- to 50-year-old person, the desirable ranges are 125 ± 15 (systolic) and 75 ± 10 (diastolic).

When blood pressure is outside the desirable range there is cause for concern. For example, a 48-year-old woman with blood pressure of 170 over 110 (170/110) has high blood pressure. Even if only her systolic blood pressure or her diastolic blood pressure were abnormal, her blood pressure would be considered abnormal. But if her blood pressure were 140/80, her pressure would be considered within desirable limits for her age.

It is possible for a person to have hypertension and not know it. This is one reason why annual checkups including blood-pressure measurements are recommended for individuals over 40. Once discovered, hypertension can be improved with drug therapy and with a low-sodium diet.

Hypertension that continues untreated for a long time may lead to serious heart disease. As we have mentioned, the most common cause of hypertension is constriction of the arterioles. It requires more work to push an adequate supply of blood through constricted arterioles. The net effect of hypertension is that the heart must work harder to pump blood. When the heart works harder, the muscular wall of the left ventricle enlarges. Over a period of time, the muscle cells in the wall of the left ventricle increase in size, so that more oxygen is needed for these cells to operate. This increases the demand on the coronary arteries, which supply blood to the heart walls. If they become partially occluded (blocked) in some way, they can't deliver enough blood. Normally the heart does not use up all the oxygen the blood brings to it. Therefore, even if there is a partial occlusion of a coronary artery the heart may still receive enough oxygen to meet its needs. In someone with hypertension, however, the heart may be using up nearly all of the oxygen in order to function. Because of this, even a slight reduction in blood flow may deprive the muscle of enough oxygen. Thus partial occlusion of a coronary artery is much more dangerous among those with hypertension than those who are free from it.

Occlusion of a coronary artery is the most common cause of death in the United States. By depriving the heart muscle of oxygen, occlusion causes heart attack. To make matters worse, hypertension is also known to increase the risk of having a coronary occlusion.

What is the difference between systolic and diastolic blood pressure?

Why is low blood pressure dangerous?

What is meant by a blood pressure of 105/65?

Why was Mr. Samuels given drugs? Speculate on why Mr. Samuels was given oxygen.

What is hypertension? Why is it dangerous?

List two conditions that result in hypertension.

What is the usual relationship between blood pressure and age?

Why is it recommended that people over 40 have an annual blood pressure check?

Why does prolonged hypertension often lead to heart disease?

Vocabulary:

diastole (die-AS-tuh-lee)--the time during which the ventricles are relaxed and are filling with blood, between heartbeats.

diastolic blood pressure (DY-uh-STAHL-ik)--the blood pressure during diastole. It is the lowest arterial pressure.

systole (SIS-tuh-lee)--the time during which the ventricles contract and pump blood into the arteries. Each heartbeat occurs during systole.

systolic blood pressure (sis-TAHL-ik)--the blood pressure during systole. It is the highest arterial pressure.

SECTION 7: HEART RATE AND CARDIAC OUTPUT

7-1 The Changing Heart Rate

What enables the heart to adjust its rate?

Carl was a heart. But he wasn't just anybody's heart. He beat proudly in the chest of Elmira Lagoon. You may wonder why Ms. Lagoon's heart had a man's name. Ms. Lagoon was fond of her heart, so she nicknamed it for her favorite actor, Carl Gnarl.

One morning Elmira was sleeping. Hammer, her dog, started barking, so Elmira woke up from pleasant dreams. She stood up. This simple act made blood suddenly start to drain from her brain, head and neck down into her abdomen and legs.

As soon as this started happening, Carl beat faster! That way he pumped more blood out, including more to Elmira's head so she wouldn't faint from lack of blood to the brain. As a matter of fact, humans are quite unusual in that they have a cirulatory system that permits them to stand erect indefinitely without losing consciousness.

What made Carl beat faster? Two nerves run from Elmira's brain to Carl. One nerve, the vagus nerve, secretes a chemical into Carl that slows down his rate. The second nerve, which we might call the "accelerator" nerve, secretes a different chemical, which makes Carl beat faster. (The "accelerator" nerve is actually a group of nerves, all secreting the same chamical. For convenience, we call this group a nerve.)*

When Elmira stood up, nerves in two arteries in her neck sensed the blood pressure dropping and sent that information to the brain. Her brain then sent more signals down the "accelerator" nerve to make it secrete more of the heart-speeding chemical into Carl. At the same time, the brain sent fewer nerve impulses down the vagus nerve, so there was less of the heart-slowing chemical secreted. These two effects increased the rate at which Carl beat.

During excitement and exercise, the heart rate increases for a second reason, too. A hormone called epinephrin (adrenalin) is secreted then by the body and it increases the heart rate. It is secreted by organs called adrenal glands, which sit on top of the kidneys. Other chemicals that speed the heart rate are the nicotine in cigarettes and other tobacco products, and the caffeine in coffee and tea.

7-2 Factors Affecting the Cardiac Output

When does the heart pump more blood?

Carl, as we said, spent his days and nights beating in Elmira. Let's look in on him one morning. Elmira was sleeping. Carl beat quietly. Each time he beat he forced out 70 ml of blood from each ventricle. The 70 ml is called his stroke volume.

Elmira always ate a big breakfast. It meant work for Carl. He pumped more blood into her stomach and intestines so those organs could digest the food. To do this, Carl increased his stroke volume. In fact, after you eat, your stroke volume can go up 30 per cent.

Elmira had stayed up late the night before. Did she have fun! Now she took her time over breakfast trying to wake up. Then she had to run to make the bus. This

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*The heart actually can beat without nerves. In experimental animals, if a beating heart is removed and placed in water containing dissolved nutrients, the heart will continue to beat. However, the nerves are important because they speed up and slow down the heart rate when necessary.

really put a load on Carl. Not only did he beat faster, he also increased his stroke volume. That meant he pumped out a lot more blood every minute than if Elmira were just resting. Let's see how much more.

Elmira running: Carl beats 150 times a minute. His stroke volume is 90 ml/beat. So Carl is pumping 90 ml/beat times 150 beats/minute, or 13,500 ml/minute. Elmira resting: Carl beats 70 times/minute. His stroke volume is 70 ml/beat. So Carl is pumping 70 times 70, or 4,900 ml/minute.

In other words, Carl pumps out almost three times as much blood per minute when Elmira is running as when she is resting. The hearts of some people can even pump up to seven or eight times as much which is 35 to 40 liters/minute. This measure, the volume of blood pumped per minute, is called the cardiac output. In someone sitting or lying down and relaxed, the cardiac output is about 5 liters/minute. Here is a list of things that change the cardiac output from this value.

INCREASE	DECREASE
•eating (30%)	•sleep
•anxiety, excitement (50-100%)	•standing up (20-30%) (even though the heart rate increases, the cardiac output is still temporarily lower)
•exercise (up to 700%)	•severe loss of blood
•pregnancy (late)	••severe dehydration
•high external temperature	•heart disease

What causes the cardiac output to go up during exercise? The main thing is that more blood is returning to Carl from Elmira's veins, so Carl has more blood he has to pump out. But why should Elmira's veins bring back more blood? Remember that blood moves in veins from the legs up to the heart when veins are squeezed by moving muscles. When Elmira runs, her muscles push on veins more, so more blood is returned to her heart. Furthermore, the brain sends signals to veins, through nerves, to become narrow. This also squeezes more blood to the heart.

Carl has two tricks up his sleeve to pump out the extra blood. First, his heart rate rises. This is caused by the activity of the nerves and the hormone epinephrin. A faster heart rate helps pump out more blood. The second thing that enables the heart to pump more blood is that each heartbeat is stronger. Each heartbeat therefore pumps out more blood, so that the stroke volume rises. This too is the result of the activity of the nerves and the hormone epinephrin. Thus, the ways in which the heart can increase its cardiac output are (1) by increasing the stroke volume, (2) by increasing the heart rate or (3) by increasing both. Usually the last happens.

What makes the nerves give the signals to speed up? The excitement of exercise (even just anticipating exercise) causes the brain to send impulses down these nerves. Also, low blood oxygen and high blood carbon dioxide, which occur during exercise, directly stimulate the brain to raise the heart rate by sending signals down the nerves. (The brain also sends signals down the nerves that control breathing rate to speed breathing up, too.)

What if Elmira were a track star? Trained athletes do not have to rely on as great a heart rate to increase their output as untrained people do. In the course of training, the stroke volume of the heart rises. Trained athletes thus have a larger stroke volume than the untrained, both during exercise and at rest. This is why trained athletes can get by with a slower heart rate. Since they have a greater stroke volume than untrained people, their heart rate does not need to be as high to pump out the same volume of blood per minute.

What if Carl were transplanted? If Carl were used to replace someone else's heart (Elmira would have to die first), he couldn't be hooked up to his new person's nerves. So there would be no way for the new brain to tell Carl to beat faster. But he could still beat faster because of the hormone epinephrin, which reaches the heart via blood.

What is meant by the stroke volume? The cardiac output?

By which nerves does the brain control h[illegible] rate?

Under what conditions does cardiac output increase? Decrease?

Speculate on the advantage of a higher cardiac output in pregnancy.

Why does more blood return to the heart during exercise? How does the heart manage to pump out this blood?

How do the hearts of trained athletes, with a slower heart rate, manage to pump out the same amount of blood per minute as untrained people's hearts?

Vocabulary:

cardiac output--the volume of blood pumped by the heart in one minute.

epinephrin (EH-pih-NEF-rin)--the hormone secreted during excitement and exercise. It increases the heart rate. It is also known as adrenalin (uh-DREN-uh-lin).

stroke volume--the volume of blood ejected from each ventricle during contraction.

vagus nerve (VAY-gus)--the nerve running from the brain to the heart which carries impulses responsible for decreasing the heart rate.

SECTION 8: THE ELECTROCARDIOGRAPH

8-1 The Pacemaker of the Heart

What is the source of the heartbeat?

In previous lessons you studied heart rate, ballistocardiography and blood pressure. Each of these is an important measure of heart function. Yet the most informative measurement of the heart's activity is made by another instrument, the electrocardiograph. This widely utilized instrument records the electrical activity of the heart. In order to understand how this instrument works, we need to consider the effect of electricity on muscles.

Figure 1 shows a laboratory set-up for testing reactions of muscle tissue. A muscle is removed from the leg of an animal and hung with a weight on its end (Figure 1A). If you pass current from a battery through the muscle, the muscle shortens and lifts the weight up (Figure 1B). In your body your nerves act like the wires in Figure 1 in bringing current to your muscles. But the heart is different from a battery. Even if a frog's heart is taken out of its body (thus disconnecting it from nerves), it keeps beating for a while. Where does the electric current in the heart come from? From the heart itself!

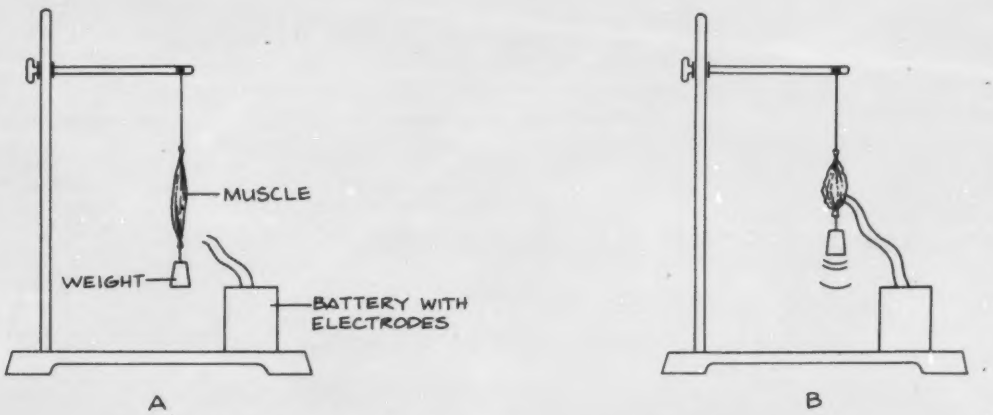


FIGURE 1: A set-up to test muscle reactions.

A. Wires from the battery do not touch the muscle. Muscle is relaxed.

B. Wires from the battery touch the muscle. The muscle contracts.

Within the heart's wall there is a special group of cells called the sinoatrial node (SA node) which releases electrical impulses (Figure 2). Each time it does, the current or activation wave, spreads through the heart-muscle tissue to make it contract. This contraction is what is known as a heartbeat. Note that the heart responds to the activation wave just as the leg muscle in Figure 1 responds to an electrical current--both muscles contract.

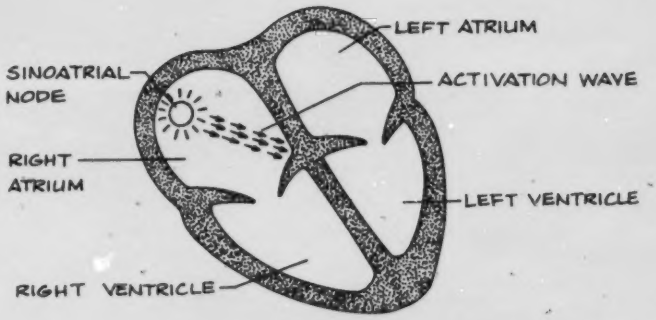


FIGURE 2: How the heart releases an electrical impulse.

The sinoatrial (SA) node is called a pacemaker because it controls the rate (or "pace") at which the heart beats. If the pacemaker fires 70 times a minute, then the heart beats 70 times a minute. Every time the pacemaker fires, the heart beats about 0.2 second later.

Sometimes heart tissue dies after a heart attack. If a particular region of heart tissue dies, the pacemaker impulse is blocked and the basic heart rhythm takes over. This is much slower than normal, about 30 beats per minute. As a result, the body will receive insufficient blood and the victim becomes weak and dizzy. In some cases the heart rate can be increased to normal with drug therapy. If drugs fail, surgery may be undertaken to wire an electrical device to the heart. This device releases electrical impulses at the same rate as the heart's normal pacemaker, and is called an "artificial pacemaker." The device is surgically implanted under the skin and connected by wires to the heart. The artificial pacemaker is battery-powered, and the batteries wear out every few years. As shown in Figure 3, the pacemaker is located some distance from the heart so that a surgeon can replace it easily, without interfering with the rib cage. Artificial pacemakers have been used very successfully. Over 100,000 Americans live with these pacemakers, and continue a normal life.

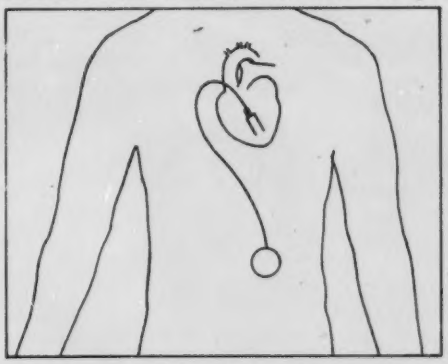


FIGURE 3: Location of the artificial pacemaker.

8-2 The Electrocardiogram

What does the ECG measure?

During the first decade of this century, a Dutch physiologist named Willem Einthoven invented a machine to record the electrical activity of the heart. It is called an electrocardiograph. The graphical record made by the machine is called an electrocardiogram. Both the graph and the machine are abbreviated ECG or EKG. (In Dutch, "cardio-" is spelled "kardio-".) The electrical impulses of the heart, picked up by electrodes attached to the body, are converted into the mechanical motion of a pen. The larger the impulse the larger the deflection of the pen. The actual ECG patterns depend on how electrodes are attached to a subject. In the following discussion, assume the electrodes are attached to a person's right arm and left leg.

Your entire heartbeat takes a little less than a second. During that time, current in the heart changes direction. First it travels from the SA node through the atria, mainly in a left downward direction. This causes an upward deflection on the ECG which is called a P wave. (See Figure 4 on the following page.) Next, the electrical or activation wave moves to the ventricles. During this stage the ECG shows a large upward deflection, called an R wave. This is the largest wave of the ECG. The valleys on both sides of the R wave are called Q and S waves. The combination of all three is called the "QRS complex."

After the current has swept through the ventricles, a final wave of electrical impulses sweeps through the heart preparing the ventricles for the next activation wave. This current creates an upward curve called a T wave in the ECG (Figure 4).

Summary of the ECG:

The P wave represents the activation current in the atria.

The QRS complex represents the activation current in the ventricles.

The T wave represents a current that prepares the ventricles for the next activation current.

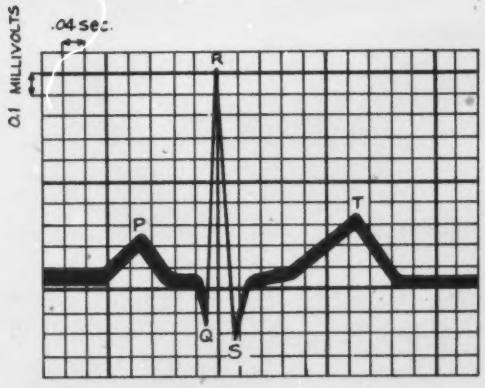


FIGURE 4: Electrocardiogram of a normal heart, with electrodes attached to the right arm and left leg.

8-3 How Do Doctors Use the ECG?

What can be done to avoid a heart attack once coronary artery disease has been diagnosed?

Heart muscle supplied by partially clogged coronary arteries does not get ample blood, and is unable to conduct current normally. This often makes the ECG abnormal. Other things affect the ECG, too, such as the K^+ ion concentration of the blood, certain vitamin deficiencies, inflammation of the sac around the heart (the pericardium) and high blood pressure. An area of the heart wall where arteries suddenly become clogged can have a special current, called the current of injury. It makes a bizarre ECG, such as the one shown in Figure 5. Compare this pattern to Figure 4.

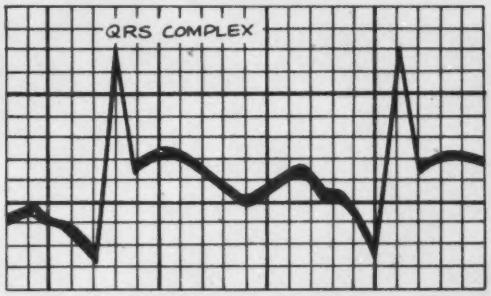


FIGURE 5: A current of injury in the ECG. The QRS complex is abnormal.

In patients who recover from heart attacks, ECG's are routinely made (Figure 6). If a particular region of the heart is destroyed by a heart attack, the activation wave from the atria can't get to the ventricles. Therefore, the ventricles do not beat as often while the atria continue at a normal rate of 65 to 90 beats per minute. So the ECG shows a normal P wave rate for the atria but less frequent QRS complexes for the ventricles (Figure 6). An artificial pacemaker wired to the ventricles can be used to increase the ventricular rate.

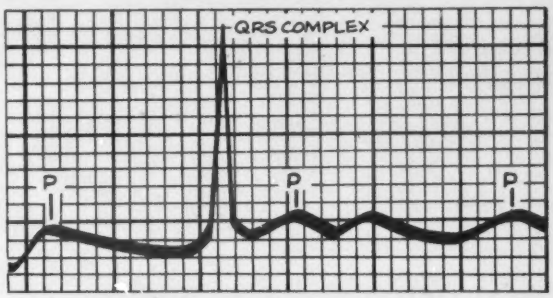


FIGURE 6: Typical ECG for some survivors of heart attacks. The P waves are more frequent than the QRS complexes because the activation current isn't getting through to the ventricles.

What causes the different chambers of the heart to contract?

Where does the activation wave of the heart begin? Where does it go?

What is an artificial pacemaker? When is it needed?

Describe what is happening in the heart during the P wave, the R wave and the T wave of the ECG.

What types of abnormalities can be detected with an ECG?

Vocabulary:

activation wave--the electrical wave which, in passing through the heart, causes the chambers to contract.

electrocardiogram--the tracing made by an electrocardiograph.

electrocardiograph--a device used to record the electrical impulses produced by the heart.

pacemaker--a structure which controls the rhythm and rate of the heartbeat.

sinoatrial node (SY-no-A-tree-ul)--the primary pacemaker of the heart, located in the upper wall of the right atrium.

SECTION 9: HARDENING OF THE ARTERIES AND HEART ATTACK

9-1 Atherosclerosis and Coronary Disease

As we have already discussed, the leading cause of death in the U.S. in the age group 36 and over is coronary heart disease (CHD). This statistic may not seem relevant to a student twenty years younger, because noticeable CHD is relatively uncommon among people between 15 and 24 years old. But it is important to remember that CHD develops slowly over a period of many years. The early stages of atherosclerosis, before it becomes serious enough to cause heart disease, have been found in the arteries of many teenagers.

Fortunately, the risk of CHD can be reduced by taking precautions beginning early in life. Many of these precautions involve the diet and have been described, in part, in the Nutrition Unit. These include reducing the intake of saturated fatty acids and sucrose. Other ways to reduce the risk of CHD include not smoking, exercising moderately, and maintaining the proper body weight.

There is good evidence that most cases of heart attack, the sudden announcement of CHD, are caused by atherosclerosis. This disease is characterized by the gradual process of arterial clogging as we discussed in Section 13 of the Nutrition Unit. Such arteries are unable to carry sufficient blood to the organ they supply. When the coronary arteries are affected by atherosclerosis, blood flow to the heart muscle is reduced and this leads to CHD.

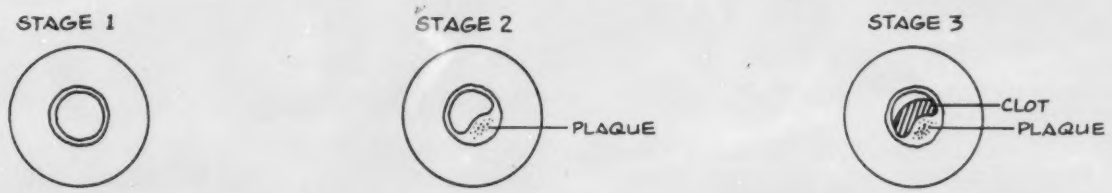
9-2 How Atherosclerosis Develops

What are the stages of development of atherosclerosis?

Over the years, it has been observed from autopsies that atherosclerosis develops in three stages. First, fats and cholesterol are deposited in the wall of the artery. Some of these deposits look like tiny dots, others are an inch or more long. They are soft, like porridge.

Next, tough fibers grow throughout the soft fat deposit. The mass of fibers extends into the cavity through which the blood is flowing. This reduces the flow a little. The fiber mass and underlying fat deposit are called a plaque (Figure 1). (You may recall that we used this term before to refer to the deposit that forms on teeth.)

During the third stage, serious problems occur. The mass of fibers that protrudes into the path of the blood traps blood cells and leads to clotting. When blood clots it gets fairly hard. Arteries in Stage 3 become less flexible and appear hard. Hence, the popular name for atherosclerosis is "hardening of the arteries."



A normal artery.

An artery partially blocked by atherosclerosis.

An artery almost completely clogged by a combination of atherosclerosis and a blood clot.

FIGURE 1: Development of atherosclerosis.

Recent evidence indicates that the process of atherosclerosis may actually be reversible, if it has not progressed too far. By following the proper steps to reduce the risk of CHD, a person may decrease the deposit of plaque in the coronary and other arteries.

A clot that forms in a blood vessel is called a thrombus. As the thrombus enlarges it blocks the flow of blood. Many different arteries can become diseased with atherosclerosis. The effect of atherosclerosis will depend on which organ the artery supplies. Arteries of the brain, heart, legs, lungs and kidneys are often affected. When the clot occurs in the coronary arteries, the disease is called coronary thrombosis. In some cases a thrombus breaks off and flows in the blood. A loose clot or other loose obstruction in a blood vessel is known as an embolus. The embolus eventually becomes lodged in a vessel too small for it to pass through. The obstruction of a blood vessel by an embolus that becomes lodged is called an embolism.

9-3 Heart Attack

How can you recognize a heart attack?

One type of heart attack occurs when a thrombus or embolus completely blocks a coronary artery. No blood can flow through the artery to the heart muscle, and the portion of the heart supplied by the artery dies from lack of oxygen. This type of attack is called a myocardial infarction (myocardium = heart muscle and infarction = death of tissue), which is often abbreviated "MI." A common misconception is that MI typically occurs during heavy exercise. In fact, it occurs more often during sleep.

The syptoms of MI vary, but the usual signs are:

- a prolonged, crushing pain in the center of the chest; or a
- severe pain which spreads to the shoulder, neck, jaw and/or arm;
- sweating;
- nausea and shortness of breath.

With improved treatment available many victims of heart attack are saved in the coronary units of emergency rooms. Treatment immediately following an MI is most important because ventricular fibrillation may occur then. In fibrillation, the heart twitches instead of beating regularly. It is fatal in minutes if not corrected, because little blood gets pumped out (Figure 2).

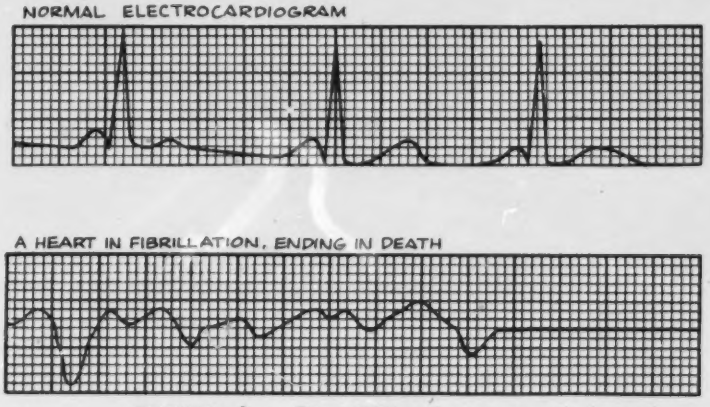


FIGURE 2: The ECG of a normal heart and a heart in fibrillation.

If the patient lives through an MI, the heart heals. But the heart is left with scar tissue where there used to be effective heart muscle. If the amount of scar tissue is not too great, the healed heart may still be an adequate pump, but there is almost always some lasting damage.

9-4 Testing for CHD

How can you tell if you have CHD?

People usually have diseased coronary arteries long before they know it. That's because the heart can perform most everyday functions with a reduced blood flow through the coronary arteries. However, it is unable to do a great deal of work under such conditions. So, while running long distances or playing hard, a symptom of coronary atherosclerosis may occur. When the heart doesn't get enough blood from its coronary arteries, a pain occurs in it called angina pectoris. "Angina" means "strangling" and "pectoris" means "chest." The pain feels like a heavy weight is pressing on the middle of the chest.

For persons with severe coronary atherosclerosis, merely walking up a flight of stairs may be enough to set off an attack of angina pectoris. This kind of heart attack

differs from MI in that the pain goes away after about 10 minutes, even without medication; and there is normally no death of heart tissue as a result of it. (It is fairly common for young people to experience sharp pains in the chest during very severe exercise. In almost all cases, these pains originate in the chest wall and should not be confused with heart or circulatory disorders.)

If CHD is suspected, a number of diagnostic tests are available which provide information about the heart and coronary arteries. The ECG, described in Section 8, is a major diagnostic tool, but it does not always detect CHD.

In many cases, disease of the arteries may not show up on the ECG when the patient is at rest. For this reason, a stress ECG may be used. In this procedure, doctors and technicians study the patient as he walks on the moving belt of a treadmill.

Figure 3 shows how a stress ECG can demonstrate CHD. Note that in this example the region between the S and T waves is abnormally depressed, an indication of CHD.

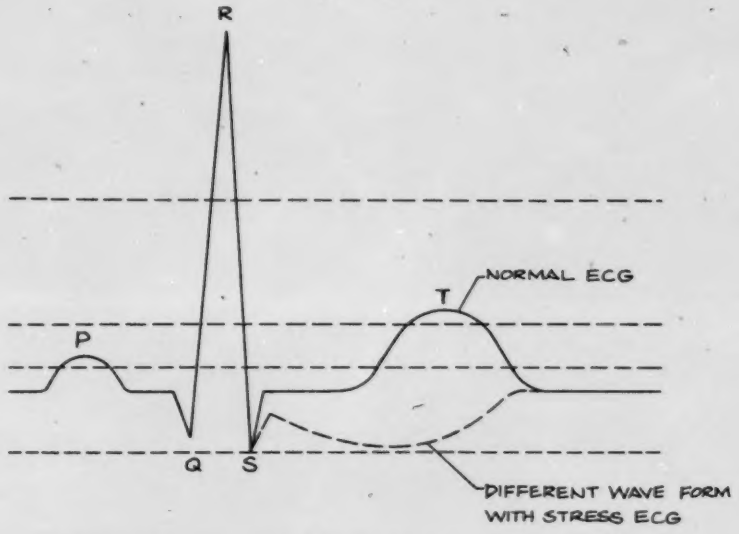


FIGURE 3: Normal ECG and abnormal stress ECG.

Another diagnostic technique, coronary angiography, consists of injecting a liquid into the coronary arteries that shows up on X-rays. At the same time, high-speed X-ray photography produces moving pictures of the liquid while it flows through the arteries. Such pictures reveal whether the coronary arteries (or other blood vessels) have been narrowed.

When the stress ECG and other diagnostic tests such as angiography indicate severely clogged coronary arteries, the physician may recommend coronary by-pass surgery. In this procedure the occluded coronary arteries are removed and replaced with veins removed from another part of the patient's body.

What are some factors that increase the risk of CHD? How can you reduce the risk of CHD?

What is meant by atherosclerosis? Describe the three stages of atherosclerosis.

In what way might atherosclerosis lead to a myocardial infarction?

What is the difference between a thrombus and a plaque? A thrombus and an embolus?

What are some of the symptoms of myocardial infarction?

Vocabulary:

angina pectoris (AN-jih-nah PEK-tor-iss)--a suffocating pain in the chest, caused by insufficient blood supply from the coronary arteries.

angiography (AN-jee-OG-ruh-fee)--a procedure for detecting narrowing of blood vessels, by means of high-speed X-ray photography of an injected liquid.

coronary thrombosis (throm-BO-sis)--the formation of a blood clot in a coronary artery.

embolism (EM-bo-lizm)--obstruction of a blood vessel by an embolus.

embolus (EM-bo-lus)--a mass of undissolved matter obstructing a blood vessel, carried there by the blood.

fibrillation (FIH-brih-LAY-shun)--irregular twitching of the heart resulting in a failure to pump sufficient blood.

myocardial infarction (MY-oh-KAR-dee-ul in-FARK-shun)--the blockage of a coronary artery, involving death of part of the heart muscle.

stress ECG--an ECG test, performed while the patient exercises.

thrombus (THROM-bus)--a clot of blood formed in a blood vessel (or the heart).

REVIEW SET 9:

1. a. Name the organ that acts as the "pump" of the circulatory system.

   b. Name the five types of blood vessels.

2. a. List at least two important functions of blood.

   b. List at least three ways in which veins and arteries differ?

3. a. How do the valves inside veins prevent blood from flowing backward?

   b. What is the role of capillaries in the circulatory system?

4. a. Why does the blood pressure drop as the blood moves along in the circulatory system?

   b. Why does the blood speed up in moving from the capillaries to the veins?

5. How is the distribution of blood to various organs controlled?

6. Why do normal cells swell up and burst when they are placed in distilled water?

7. Describe the function of each of the heart's chambers.

8. Where does the heart muscle itself get its blood supply?

9. a. What is a stethoscope used for?

   b. What are some normal situations that increase heart rate?

10. a. How do systolic and diastolic blood pressure differ?

    b. What is hypertension and why is it a medical problem?

11. What function does the vagus nerve perform in circulation?

12. What are two ways that the heart increases the volume of blood it pumps to the body?

13. What is the electrocardiograph used for?

14. What function does an artificial pacemaker serve?

15. List four risk factors correlated with coronary heart disease.

16. Describe the stages of atherosclerosis.

SECTION 10: THE NATURE OF BLOOD

10-1 Blood--The Red Fluid of Life

"Blood" is a term rich in meaning and richer still in association. At one time, people believed that blood determined our heredity and even our personality--they spoke of "royal blood" and "blue-blooded aristocracy." The red stripes on barber

poles once symbolized blood. Less than a century ago, the work of barbers included drawing blood from customers who expected such "blood-letting" to cure their diseases. Myths about blood are less common now, but the subject of blood is still a fascinating one with much left to be discovered.

In the earlier sections of this unit, the focus was on the circulatory system. Blood, of course, is the fluid that circulates through that system. In this and in the following sections, we will examine this fluid and its role in life. We will see that the functions of blood include not only transport, but also regulation of body pH and temperature (homeostasis) and resistance to infection. In addition, blood carries the factors needed for blood clotting.

10-2 Case History--Female, Age 18

Why did Betty faint?

Betty was just about everybody's favorite person. The Lincoln High yearbook described her as "popular, attractive, fun, busy" and the description fit her well. Among other things, she was President of the Senior Class, played basketball, sang with a rock band, dated three times a week and managed to keep a B+ average.

What happened to Betty in the gym class was a surprise to everybody including herself. She lay there on the hardwood floor with her eyes wide open. Why was everyone watching her? What had happened?

"You were out," someone said.

The P.E. teacher looked down at her. "How are you feeling, Betty? You fainted."

Betty felt okay, but a little dazed and puzzled. She had never fainted before, although lately she had been having occasional dizzy spells. The teacher insisted that Betty see her physician.

* * *

Dr. Gray had a lot of questions to ask and he went at it quickly. He asked whether she had fainted before. She explained that she hadn't, but mentioned her dizzy spells. She thought this was because she had been overworking herself and not getting enough sleep. Dr. Gray asked questions about her daily routine. "Have you felt fatigued lately? Do you tire easily? Do your muscles ache?"

"Well, Doctor," she said, "I'll admit I feel like I've had it sometimes and I can hardly get up in the mornings. I feel sore all over. But then I'm awfully busy--all my activities, you know--and I have to cook dinner and take care of the kids a lot because Mom works late. It's no wonder I feel tired all the time."

The physician listened, took occasional notes, and continued his questioning. He asked whether Betty ever had difficulty breathing. She said she had felt short of breath in recent months whenever she had to do vigorous exercise. The doctor looked at her fingernails and then asked if she noticed whether her complexion was paler than in previous years. She recalled that her mother had complained that she looked pale lately. She wasn't convinced.

Dr. Gray then asked questions about loss of blood. If you cut yourself, do you bleed for a long time? (No.) Were you in an accident lately? (No.) Do you have heavy menstrual flow? (Yes.) Did you lose blood for any other reason recently? (No.) The doctor paused and explained that he needed to know whether there was any possibility that she was pregnant. (None.)

The physician continued with his note taking. He measured her height and weight and noted that she was a little underweight. "Let's talk about food," he continued. "I want to know what your diet is like."

"Pretty bad," she responded, "I'm an awful cook and too rushed to worry about nutrition." She went on by describing some typical meals.

Dr. Gray commented that her diet included little meat or green leafy vegetables and Betty agreed. He started to raise another question about diet, but Betty interrupted, "Doctor, all I did was faint. I feel tired but otherwise pretty good. Why all this concern?"

The doctor smiled. "Good question," he said. Let's review some things you've told me about yourself, and then we'll let you be the physician. Your patient is an overworked, eighteen-year-old girl who just fainted. She is pale, underweight and tired, and she has dizzy spells. Her diet is poor and..."

"Anemia?" she blurted out, surprising herself.

"Very good, Doctor," he chuckled. "Because of the symptoms, we should suspect anemia. Actually, there are many kinds of anemia. If we confirm that you are anemic, we would then have to find the underlying cause to design the correct treatment. Anemia may have a dietary cause--insufficient iron or vitamin B_{12}. It may also be due to loss of blood, and there are still other possible causes."

Dr. Gray caught his breath and then said, "On with the exam!" He proceeded to review Betty's health history. He wanted to know if she were a heavy smoker. (No.) He inquired about the medical background of her immediate family. The doctor was concerned about the possibility of an inherited anemia.

The physician then gave Betty a thorough physical checkup: he checked for swollen glands, listened to her heart with his stethoscope, palpated her bones, looked at her tongue, and so on. He ended the examination by drawing five milliliters of venous blood and said, "The blood is for the laboratory. It isn't much blood, but you will be amazed at how much it can tell us. Come back next Thursday when I have some results from the lab. In the meantime, I want you to get more rest and pay more attention to your diet."

* * *

On Thursday when Betty came back, Dr. Gray smiled and told her she was anemic. Her blood hemoglobin was low for her sex and age but she was lucky! Her kind of anemic was easily curable with proper diet. The examination and the lab tests had ruled out the more serious kinds of anemia. He gave her a prescription for some iron tablets and suggested that she or her parents speak to Mrs. Schwartz, a dietician that he knew at the hospital.

10-3 Blood Cells

What kinds of cells are found in blood?

The diagnosis of Betty's anemia involved careful laboratory analysis of her blood. To understand the diagnosis, we must investigate the nature of blood. No doubt, you've seen blood many times, maybe too many times--a thick, opaque, brilliant red fluid. It is slightly more dense than water and appears to be homogeneous (that is, uniform in make-up). The illusion of homogeneity disappears on further study. For instance, if we put some blood in a centrifuge tube (along with a small amount of a substance to prevent clotting) and spin it down for a few minutes, two distinct fractions are produced. The upper fraction is a yellowish fluid called plasma and the dense red fluid that settles is called the formed elements (see Figure 1).

BLOOD = PLASMA + FORMED ELEMENTS

FIGURE 1: Components of blood.

The formed elements of blood are very interesting to look at in the microscope. If we examine a drop of this material under a high-power microscope, the first thing we note is an enormous number of cells that look something like minute doughnuts. Although these cells are pink individually, when crowded together they give blood its characteristic color; so they are called red blood cells or erythrocytes (Figure 2). And crowded together they are! In 1 ml of blood from an adult male there are about 5,000,000,000 (5×10^9) red blood cells. (Adult women have slightly fewer red blood cells per ml.) If this doesn't impress you, you might try to calculate how long a chain you would have if you lined up all your red blood cells from end to end. Hint: 1200 erythrocytes would give you one cm. Also, you have about 24 trillion (24×10^{12}) red blood cells altogether.

Now, back to the formed elements and the microscope. If we looked very carefully, we would occasionally see cells that differ from red blood cells. For every 500 or so red blood cells, we would see one cell that looks different. This is a white blood cell, or leukocyte. To analyze blood cells, medical technicians use staining techniques. After staining, it is easier to see that the white cells are of different sizes and shapes. There are many different kinds of white blood cells. There is also an additional component of the formed elements called the platelets. (These tiny structures are really fragments of cells.) The stains make it possible to distinguish all three classes of formed elements (Figure 2). We will consider each class of formed elements in the sections that follow.

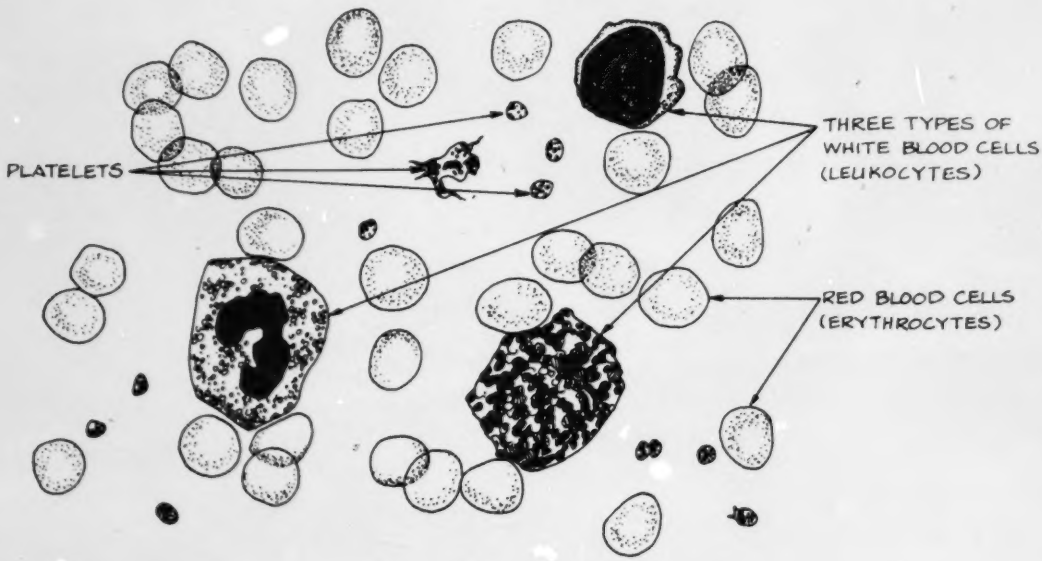


FIGURE 2: The cellular components of blood.

Blood cells have a great deal of clinical significance. For example, in Betty's case, a finding of smaller and paler red blood cells would have helped to confirm the diagnosis of iron-deficiency anemia. Similarly, abnormal numbers of blood cells provide clues to many diseases. We will consider several blood diseases in later sections.

What functions are performed by blood?

What were the clues that led to a diagnosis of nutritional anemia in the case history?

Why did Dr. Gray ask Betty about menstrual bleeding? Why was he concerned about Betty's diet?

What would you see if you looked at formed elements of the blood with a microscope?

How would you obtain blood plasma from a sample of fresh blood?

Vocabulary:

erythrocyte (e-RITH-ro-site)--a red blood cell.

formed elements--the cellular components of blood.

leukocyte (LOO-ko-site)--a colorless blood cell.

palpate--to examine and diagnose by touching.

plasma (PLAZ-muh)--the fluid part of the blood.

platelet (PLATE-lit)--a small colorless cell fragment found in blood.

white blood cell--same as leukocyte.

SECTION 11: DIFFERENTIATION AND FUNCTIONS OF BLOOD CELLS

11-1 The Case of the Coed Who Fainted--Epilog

Dr. Gray sat at his desk pondering after the long day. He pictured the many faces that had passed before him and recalled the things he had heard. He thought about age and youth.

"The great thing about youth," he thought, "is the elasticity. My young patients are like rubber balls--they bounce back so quickly."

He was thinking about Betty and the good report from the lab he had before him. It had been only two months since he recognized her iron-deficiency anemia and already she was a changed person. The pallor of anemia was gone, along with the other symptoms--the fatigue, the dizzy spells, the vague muscle aches. She had gained a few pounds and seemed less tense, happier. Now her hemoglobin concentration was in the normal range. Blood stains suggested that recovery was complete.

He studied the lab report. The erythrocytes were no longer small nor were they as pale as before. He filed the report and left the office with a good feeling.

11-2 The Birth and Death of an Erythrocyte

What do blood stains reveal about the development of a red blood cell?

You already know a number of things about erythrocytes (red blood cells). These important cells (1) have an unusual shape, (2) constitute over 90 per cent of our blood cells, (3) contain virtually all of our hemoglobin, and (4) carry oxygen to all parts of the body. If we are to appreciate the role of the laboratory in the diagnosis of anemia, we need to know more about red blood cells.

Imagine that we could look at a single red blood cell in a person and watch this cell for several months. The erythrocyte would circulate through the bloodstream for a period of time and eventually die. Death comes to the average red blood cell in about 120 days. That the cell dies is not surprising. Cells are "born" (by cell division), they age and they die. It is a little surprising that erythrocytes die as quickly as they do (most cells live much longer), and it is even more surprising how they die. Old red blood cells are killed by large cells in our livers and spleens, which surround and digest them just as an ameba digests its food. These large cells, or macrophages, practice a sort of cannibalism which removes older and damaged erythrocytes from the bloodstream.

The erythrocytes are devoured by macrophages at an astronomical rate; in one minute over 100,000,000 are destroyed. To avoid anemia, we must produce new erythrocytes at a similar rate. The erythrocyte is the end-product of a metamorphosis (change) as striking as the one that produces a butterfly. The cellular process

is called differentiation. It is the process by which a cell changes in shape and structure, and becomes more specialized to perform a function.

The processes of differentiation and specialization are not limited to erythrocytes. In fact, a human being starts as a single cell (i.e., a fertilized egg cell) which divides many times until, at birth, there is an enormous number of cells of different sizes and shapes--nerve cells, skin cells, muscle cells and so on. The process that produces all of these different kinds of cells from a single original cell is differentiation. Much of the differentiation in humans occurs before birth. However, erythrocytes are made continuously throughout the lifetime of the individual.

A diagram of some of the stages in the differentiation of an erythrocyte is shown in Figure 1. To observe this differentiation, we need to make blood smears and stain the cells. A few drops of blood are spread ("smeared") over a slide and then a stain is added. Wright's stain is especially useful because it stains the nucleus of the cell and also any structures in the cytoplasm (all of the cell except the nucleus).

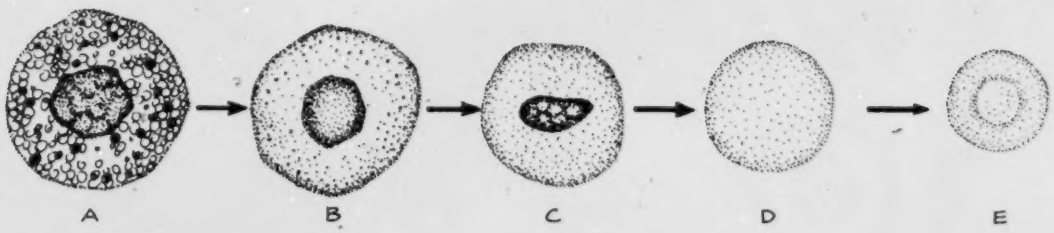


FIGURE 1: Differentiation of an erythrocyte.

In the differentiation, a few major trends may be observed by studying blood smears. The most obvious is that the size of the cell and of the nucleus decreases. The stained nucleus darkens; and when a cell goes from stage C to D (Figure 1) the nucleus is broken down and a network is left behind. This network includes the enzymes needed for making hemoglobin. In the erythrocyte (Stage E), this network is also broken down. Thus the erythrocyte lacks both the network and the nucleus and cannot make hemoglobin.

When you stain blood cells in laboratory Activity 11, you will not see most of the kinds of cells shown in Figure 1. Of the five kinds of cells shown, you will probably find only erythrocytes. You may see very small numbers of the cells labeled as Stage D. This is normal. But in iron-deficiency anemia, more of these cells, and sometimes Stage C cells, are found in blood smears.

If the cells that give rise to erythrocytes are not in the blood, then where are they? These cells are produced in the bone marrow. Erythrocytes and some cells in Stage D pass from the bone marrow to capillaries and into the circulatory system. The Stage D cells lose their network in a few days. Once the network is lost, an erythrocyte is born.

Blood stains are used to diagnose other forms of anemia as well. In sickle-cell anemia, the erythrocytes can become distorted when oxygen is in short supply. The strange cell shapes that form are behind the name--some of the cells look a little like a sickle--an old-fashioned farm implement (Figure 2). In an anemia that results from vitamin B_{12} deficiency, the blood will contain cells in stages B and C of differentiation.

FIGURE 2: Appearance of red blood cells in sickle-cell anemia.

11-3 The Structure and Function of the Erythrocyte

How is the lack of a nucleus useful in the erythrocyte?

In the development of the erythrocyte, the most remarkable event is the disappearance of the nucleus. The ability of a cell to live without a nucleus is surprising, for the nucleus is considered to be the most important part of a cell. It serves as the cell headquarters controlling all of the activities within a cell. Yet the erythrocyte has no nucleus!

Recall that an important function of the erythrocyte is to carry oxygen to all parts of the body. So why would oxygen transport be more efficient in a cell without a nucleus? Cell biologists suspect that the solution may be very simple. Without the nucleus, there is more room for hemoglobin molecules which actually carry the oxygen. In fact, the concentration of hemoglobin in the erythrocytes of man has been compared with the concentration in organisms such as chickens. (In chickens the erythrocytes do have a nucleus.) These comparisons show that even though the chicken has a larger erythrocyte, the chicken red blood cell carries less oxygen than the human red blood cell.

The flattened shape (Figure 3) is also thought to be advantageous. It is believed that this shape places most of the hemoglobin molecules near the cell membrane. This makes it easier for the exchange of oxygen (and carbon dioxide) to occur than in a more nearly spherical cell.

FIGURE 3: Red blood cells.

The relation of the shape of an erythrocyte to its function is another example of adaptation. We have already seen adaptation in the circulatory system (e.g., the extremely thin walls of capillaries), digestive system (e.g., the very long tube that makes up the intestines) and the respiratory system (e.g., the huge surface area of the alveoli). However, the adaptation of the erythrocyte is the first example we have considered on the cell level rather than the organ level.

11-4 Leukocytes and Their Diagnostic Value

What else can we learn from blood smears?

Just as blood smears are used to study erythrocytes, they may also be used to study the white blood cells (leukocytes) and platelets in our blood. Unstained leukocytes are colorless and hard to distinguish from one another; but by staining, we find a surprising variety of cells. They come in assorted sizes, shapes and colors--purple, blue, orange. Figure 4 shows a few of the many kinds of leukocytes and how they appear on a blood smear. Generally, leukocytes are larger than erythrocytes (also shown in Figure 4). The different classes of leukocytes may be distinguished by differences in the colors of their cytoplasm and nuclei. The shape of the nucleus and the presence or absence of granules in the cytoplasm is also useful in classification.

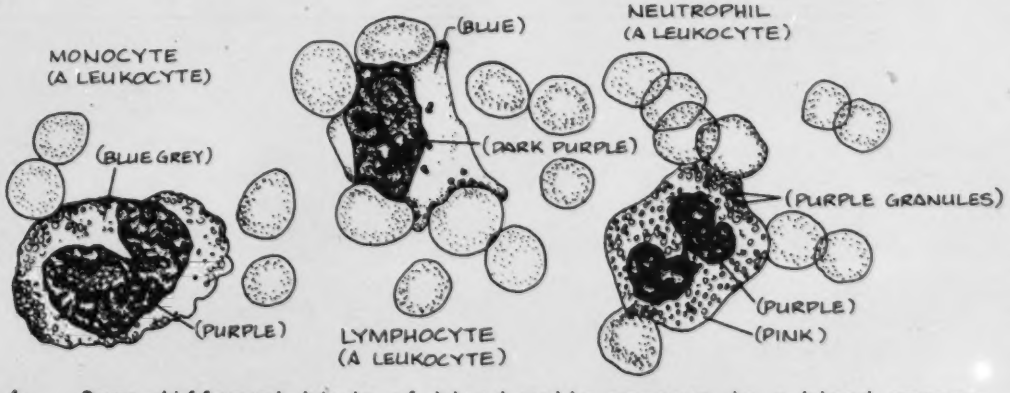


FIGURE 4: Some different kinds of blood cells as seen in a blood smear.

Stained blood smears give important clues for the detection of all sorts of clinical problems ranging from malaria to lead poisoning, allergies, viral infections and leukemia. For example, the presence of abnormal white blood cells might be an early indication of blood poisoning or it might be a clue to a perforated ulcer. In infections, the white blood cell count goes way up. Millions of these blood cells congregate with living and dead bacteria and dead tissue to form that thick yellowish fluid you have no doubt seen--pus.

Why are blood smears important in a diagnosis of anemia?

What is accomplished by cell differentiation?

What is the principle function of an erythrocyte? How is its flattened shape adapted to its function?

Why is it important to study leukocytes as well as erythrocytes in blood smears?

Vocabulary:

cytoplasm (SY-toe-plazm)--the cellular material outside of the nucleus.

differentiation--the process by which a cell becomes more specialized.

macrophage (MAK-ro-fayj)--a large cell, found in the liver and spleen, that destroys old erythrocytes.

SECTION 12: BODY FLUIDS AND EDEMA

12-1 Body Fluids in Compartments

Where is the water in our bodies?

We tend to think of ourselves as "solid citizens," but in fact we are more liquid than solid. An average 150-lb person carries about 90 lb of water and only about 60 lb of solids. Our water content depends on age, sex and other factors. For example, an obese person has a lower percentage of water than a lean person because fatty tissue contains little or no water.

When you think about it, it is not surprising that we contain so much water. Without water or a comparable fluid in our bodies, most metabolic reactions could not occur, necessary biochemicals could neither reach nor diffuse into our cells, our body temperature could not be regulated, and so on. In short, water is crucial to our survival.

Where is all this body water contained? A reasonable guess would be the blood. But only seven per cent of our body water is found in the blood. The bulk of the water is within our cells (71 per cent) and accounts for most of the intracellular fluid. The rest (22 per cent) surrounds our cells and is in the interstitial fluid. Such terms are easier to understand if you remember that "intra-" means "within" and "inter-" means "between." An intramural league includes teams within a single school, while inter-school athletic events involve competition between schools.

Our body water is contained within three distinct compartments. The compartment that carries blood is, of course, the circulatory system. The cell is the compartment that houses intracellular fluid. Even though we have an astronomical number of cells, our bodies are more than cells and blood vessels. There is much space around the cells. This is the interstitial space that contains the interstitial fluid.

Water moves freely from one compartment to another. Thus the water you drink is soon distributed into all three compartments. Molecules and ions dissolved in water also move from one compartment to another. But they do not pass through the cell membrane as freely as water, and some substances are rejected by the cell membrane. You may recall that cell membranes do not permit proteins to pass through because proteins are too large--that the membranes of cells are selectively permeable. Other susbtances are also rejected by the cell membrane. And the selection is not

simply a matter of size. For example, substances that are fat-soluble pass through the cell membrane more readily than water-soluble compounds and K^+ ions enter a cell more readily than Ca^{++} or Mg^{++} ions. The membranes of cells are a little like a doorman at an exclusive nightclub who permits only VIP's with tuxedos to enter.

12-2 Edema--A Flaw in the Distribution of Body Fluids

What is edema? How is it caused?

The distribution of body fluids remains fairly constant in a normal individual. The distribution is regulated by homeostatic processes. But sometimes a person will accumulate excess water in the interstitial space and this is called edema. The excess water may be localized and appear as a lump ("edema" comes from a Greek work for "swelling"). If you ever got a "bump" on your head or caught a baseball on the tip of your finger, you've had localized edema. In these cases, the blow damages the capillaries making them more permeable to proteins. Plasma proteins escape into the interstitial fluid. Recall the delicate balance between the blood pressure and osmotic pressure that permits the movement of fluid into and out of the capillaries. When proteins escape from the capillaries into the interstitial fluid, this balance is upset. The result is a net movement of water into the interstitial space from the blood. As the volume of water in the interstitial space increases, the swelling that typifies edema occurs.

Another type of localized edema that you may have experienced is the kind caused by bacterial infections. Did you ever have an infected finger that swelled up? This sometimes results because the bacteria release chemical substances that make the capillaries more permeable to proteins. Again, proteins are released into the interstitial fluid and edema results.

Still another form of edema that you may be familiar with is associated with starvation. You may have seen photographs in the newspapers or on TV of pathetic, undernourished babies with swollen bellies. The bulging bellies are, in this case, not the result of overeating. On the contrary, the children are suffering from edema and their abdomens are filled with water. They have a condition called kwashiorkor which comes from a West African word meaning "disease of the first child when the next one is born." The tradition is for the first child to be switched from mother's milk to a diet of "rice water" (i.e., water in which rice has been cooked) when the new baby is born. The mother remains on a higher protein diet to produce milk. The central problem is that the child on the rice-water diet gets insufficient protein. As a result, the child has less plasma protein than usual. The protein concentration in the interstitial space is then high relative to the concentration in the blood vessels. The osmotic pressure balance is altered and water is released from the blood vessels into the interstitial space.

The presence of edema almost always indicates a serious problem. When serious CHD is present and the heart is no longer working well as a pump, a complex chain of events occur which leads to severe edema.

Modern treatment of heart disease often uses diuretics, drugs which make patients urinate more. When a lot of water is excreted as urine, more water leaves the blood and enters the urinary system. As a result, the water concentration in the blood becomes low relative to its cencentration in the interstitial space. Then the water molecules in the interstitial fluid diffuse into the blood through the capillary walls providing some relief from the edema. Many diuretics work by causing the kidneys to eliminate sodium ions. When sodium is eliminated, so is water. This explains why patients with heart disease and edema are generally placed on a low-salt diet. The diet is an important part of the therapy.

A major breakthrough in treatment of heart disease was made in 1785 by a British physician named Withering. He learned of an old woman in Shropshire who claimed to have a cure for heart disease. She fed victims of this disease a mixture of herbs including foxglove. Dr. Withering found that it was the leaves of the foxglove plant that gave relief to his patients. Many years later, it was found that a compound in foxglove was the effective ingredient. It improved the ability of the weakened heart muscles to contract. A foxglove extract is still used with many cardiac patients.

There was an old lady from Britain,
Whose story is frequently written.
From her garden, with love,
She offered foxglove,
To patients whose hearts had been smitten.

Anon.

What are the three compartments containing body water? Which compartment contains the most? Which contains the least?

What is edema? Explain how it may result from a blow or from a bacterial infection.

Explain how edema can result from kwashiorkor.

What is a diuretic? How does it relieve edema?

Vocabulary:

diuretic (DY-yoo-RET-ik)--a compound that causes a person to eliminate more urine.

edema (uh-DEE-muh)--accumulation of excess fluid in the interstitial spaces.

insterstitial fluid (IN-tur-STISH-ul)--the body fluid housed neither in the blood vessels nor in the cells.

intracellular fluid--the fluid content of cells.

kwashiorkor (KWAH-she-OR-kur)--a nutritional disease caused by a dietary deficiency of protein.

SECTION 13: CLINICAL APPLICATIONS OF PLASMA PROTEIN ELECTROPHORESIS

Electrophoresis of plasma proteins is an important diagnostic procedure for a number of diseases. It helps to confirm diagnoses based on a physical examination and other laboratory tests. You tried electrophroesis in the laboratory and, after staining, you probably obtained a pattern something like the one in Figure 1. Perhaps you found two separate areas that were stained. Each stained area constitutes a group of proteins with a similar net charge.

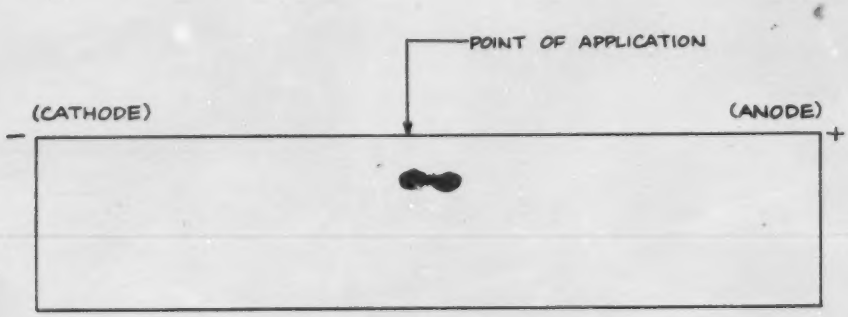


FIGURE 1: Electrophoresis of plasma proteins with the BIP.

Given more sophisticated equipment and the time to develop greater skill, you would get patterns with five bands as in Figure 2 on the following page. (In this case, the plasma was initially applied as a fine line across the entire width of the strip.) The broad band nearest to the anode is albumin. All the other bands are globulins.

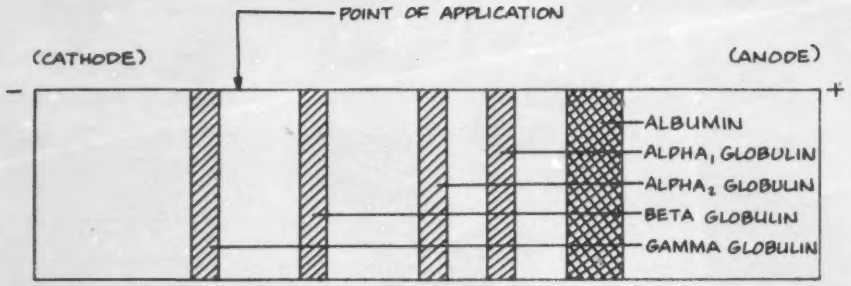


FIGURE 2: Protein bands after electrophoresis of plasma proteins.

Albumin is the most prevalent protein in blood plasma. For every 100 ml of blood plasma, there is typically about 3.7 g albumin and 3.0 g of all the globulins combined. The main function of albumin is to regulate the osmotic pressure in the circulatory system. You probably will recall from Section 12 how a decrease in the protein concentration of the plasma results in edema. While the globulins also contribute to the osmotic pressure of circulating blood plasma, they perform many other functions as well. For example, many substances bind to these proteins and are thus carried through the circulatory system to all parts of the body. In addition, the globulins are involved in immunity.

The same five bands are almost always found in plasma from both normal and diseased people. How then can electrophoresis be useful in diagnosis? The answer lies in the concentration of the various plasma proteins in normal and diseased individuals. For example, a patient with cirrhosis (a disease characterized by replacement of liver tissue by non-functioning scar tissue) has less albumin and more gamma globulin than normal individuals. This is shown in the following table. Such deviations from normal concentrations, in addition to other laboratory tests (such as urine bilirubin concentration) may indicate cirrhosis. So for clinical application of electrophoresis, it is necessary to know the concentration of proteins in each band.

Normal Range of Serum Protein Concentrations
vs. Typical Cirrhosis Patient

COMPONENT	NORMAL RANGE (g/100 ml)	CIRRHOSIS PATIENT (g/100 ml)
Albumin	3.2-5.6	2.9
$Alpha_1$ Globulin	0.1-0.4	0.2
$Alpha_2$ Globulin	0.4-1.2	0.7
Beta Globulin	0.5-1.1	1.3
Gamma Globulin	0.5-1.6	2.4

To determine the concentration of proteins in electrophoresis, a technique is used that is much like colorimetry. If you examine the electrophoretic pattern you produced, you will probably note that the bands are stained unequally. As in colorimetry the intensity of color in the bands is proportional to the concentration of the proteins. To measure the intensity, an instrument much like a colorimeter is

used. It is called a densitometer. The electrophoretic strip is mechanically moved in front of a slit through which light is passing. As the strip passes over the slit, the densitometer registers the amount of light that is transmitted through the stained and unstained areas of the strip. As the strip moves, the device automatically plots the results as a graph of % transmittance vs. distance. Figure 3 shows a typical pattern for normal plasma. The areas under the curve represent the concentrations of proteins in each band. Each band is marked by a capital letter for convenience. Note that the most prevalent protein is albumin and the least common is alpha$_1$ globulin.

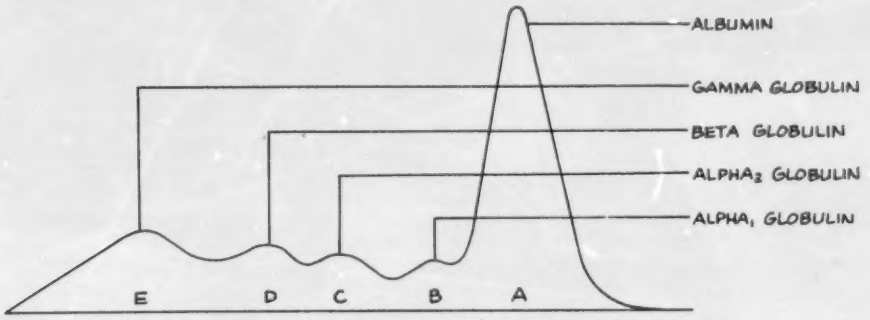


FIGURE 3: An electrophoretic pattern for plasma proteins of a normal individual.

Let's consider how electrophoresis may be used to aid in diagnosing a few diseases. These diseases have to do with immunity, which in turn is related to blood proteins. Antibodies are found in the gamma globulin fraction. The subjects of antibodies and immunology will be developed in the next section.

1. Chronic Microbial Infection--The concentration of gamma globulin increases dramatically. Electrophoresis actually reveals the results of an immunological response to the infection. Newly synthesized antibodies account for the increase of gamma globulin.

2. Hypogammaglobulinemia--Recall that "hypo-" means "less" or "too little" and "-emia" refers to blood, so the name of this disease tells you what to expect in electrophoresis. Patients with hypogammaglobulinemia show a low concentration of gamma globulin. In addition, they are unable to increase the concentration significantly in response to infection, which makes them highly susceptible to infectious diseases.

3. Nephrotic Syndrome: The term, nephrotic, comes from the Greek word for "kidney." In the nephrotic syndrome, the kidney degenerates and becomes less functional. People with this condition have peculiar electrophoretic patterns. Their albumin concentration decreases while the alpha$_2$ globulin concentration increases dramatically. An increase in the beta globulin concentration may also be found.

In electrophoresis of plasma proteins, five bands are typically found. What are these bands composed of?

What is densitometry? How can it be used as an aid in diagnosing conditions such as cirrhosis?

Vocabulary:

albumin (al-BEW-min)--the most prevalent of the blood proteins.

cirrhosis (sih-RO-sis)--A liver disease characterized by inflammation and tissue scarring.

densitometer (DEN-sih-TOM-uh-tur)--an instrument that measures the intensity of light transmitted.

globulin--(GLOB-you-lin)--a protein fraction of blood actually composed of several different subfractions of proteins.

hypogammaglobulinemia (HY-po-GAM-uh-GLOB-you-li-NEE-mee-uh)--a condition in which there is a shortage of gamma globulin.

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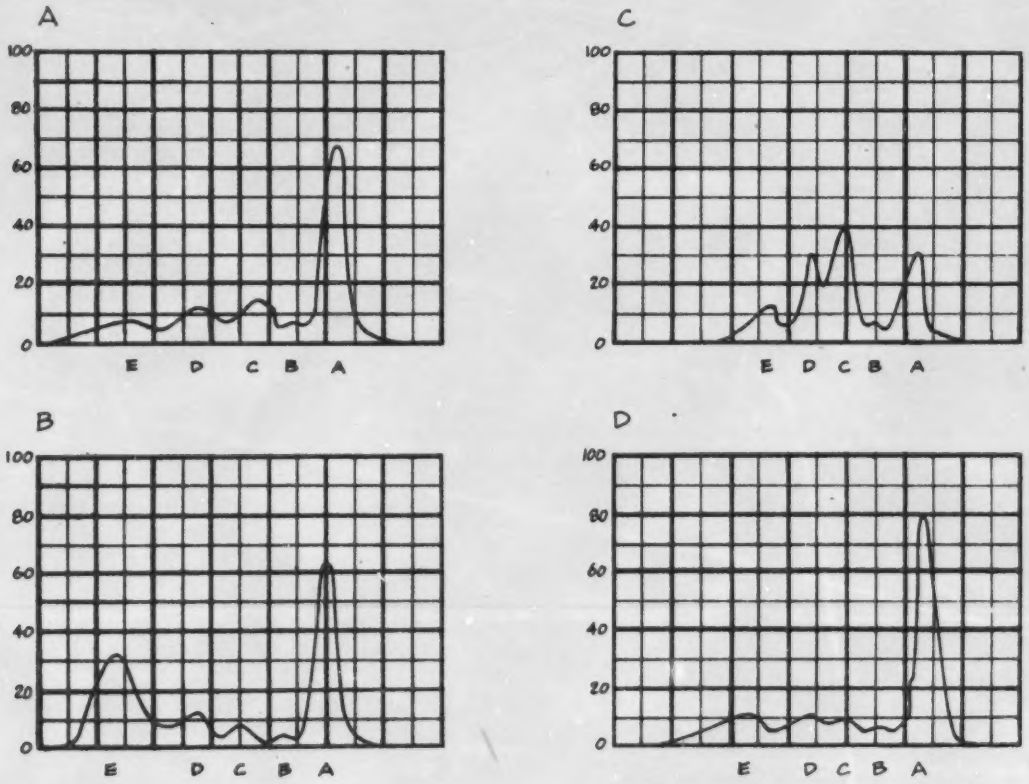
nephrotic (neh-FRAHT-ik)--pertaining to kidney disease which involves destruction of cells.

syndrome (SIN-drome)--a group of symptoms which together describe a disorder.

PROBLEM SET 13:

Four electrophoretic patterns are shown below. One of these is normal, one corresponds to chronic microbial infection, one to hypogammaglobulinemia and the last one to nephrotic syndrome. Your task is to determine which pattern corresponds to which disease.



SECTION 14: WHITE BLOOD CELLS AND THEIR FUNCTIONS

14-1 What Good is a White Blood Cell?

In Section 11 we considered the functions of red blood cells (erythrocytes). White blood cells (leukocytes) were also mentioned in that section, but their roles in the body were not considered in detail. What are the functions of the various kinds of white blood cells?

Before we answer this question, let's restate two facts about white blood cells that have already been mentioned. They provide a clue to the answer.

1. White blood cells usually increase in concentration during infection.

2. Some white blood cells can destroy pathogenic (harmful) bacteria by phagocytosis.

From these two statements, you might guess that white blood cells are involved in defending the body against infectious disease. If this is your suspicion, you are on the right track, for the main function of these cells is to destroy invading

microbes. Like soldiers, the white blood cells are organized by the body to respond to invasions by pathogens. There are several kinds of white blood cells. And each is specialized to perform a different task. Let's consider some ways in which they operate.

14-2 The White Blood Cells and Phagocytosis

How do neutrophils destroy bacteria?

In Activity 14 we mentioned that certain kinds of white blood cells can destroy pathogens by phagocytosis. The neutrophils are the most important kind of phagocytic white blood cell. A neutrophil can surround, absorb and destroy a bacterium. It does this in a way much like that of an ameba eating bacteria (Figure 1). The neutrophils move like an ameba (see arrows in Figure 1). As the cytoplasm streams in a particular direction, the membrane expands making room for the flow. The shape of the cell changes, becoming long in the direction of the flowing cytoplasm. The rest of the cell follows along behind the stream of cytoplasm.

FIGURE 1: An ameba capturing bacteria.

When the neutrophil surrounds a microbe, the microbe is absorbed into the cytoplasm of the neutrophil as in Figure 2. The microbe (including a wrapping of cell membrane from the neutrophil) is then broken down by enzymes. The neutrophil produces hydrogen perioxide (H_2O_2). In the presence of an enzyme in the neutrophil called "peroxidase," the H_2O_2 forms H_2O and O_2; and the oxygen formed kills the microbe. There is a rare disease in which humans lack peroxidase in their neutrophils and so can't kill bacteria. It is called granulomatous disease of childhood and its victims are very susceptible to infection.

FIGURE 2: Phagocytosis.

The scene of the phagocytic battleground is frequently not the bloodstream. The white blood cells (unlike the red blood cells) have the ability to pass out of the circulatory system. They squeeze out through holes in the capillary walls by taking on a filament-like shape. Once out, the white blood cells can fight infections anywhere in the body. Pus contains any neutrophils that have left the bloodstream through the capillary walls.

14-3 Other Functions of White Blood Cells

How do white blood cells contribute to immunity?

Not all white blood cells are phagocytic. For example, the lymphocytes cannot surround and absorb bacteria. Yet they are powerful weapons in the battle against microbial diseases. Lymphocytes produce proteins that are specifically tailored to react with and destroy foreign microbes (sometimes referred to as foreign bodies)--these proteins are called antibodies. In the Nutrition Unit we discussed hepatitis antibodies. The study of antibodies and related subjects is known as immunology, because antibodies make us immune to invading microbes. Immunology is a field of increasing importance in medicine. Immunologists work on health problems ranging from cancer to kidney transplants, hay fever and rheumatic heart disease.

14-4 Different Ways that Antibodies Work

How do antibodies help to prevent disease?

You may recall from Activity 14 that Almoth Wright conceived of substances related to white blood cell phagocytosis and he called the substances opsonins. Although he never proved that opsonins exist, Wright suggested that they attach to bacteria and make the bacteria more susceptible to the action of phagocytes. The writer George Bernard Shaw once described opsonins as a "natural sauce" with which "we butter the disease germs appetizingly." We now know that opsonins are real compounds--they are antibodies and are made by lymphocytes.

But opsonins are only one of several kinds of antibodies. For example, consider how antibodies help protect us against tetanus. Tetanus is a frequently fatal disease that results in a variety of very severe symptoms, including extreme rigidity of the body. (This explains its popular name, "lockjaw.") The disease is caused by a toxin made by Clostridium tetani. If someone gets infected with a small number of the tetanus bacteria, they may not show any symptoms of the disease. But the toxin molecules may come in contact with lymphocytes. If this happens, the lymphocytes will make and release antibodies into the blood plasma which can inactivate the toxin. Such antibodies are called "antitoxins."

Most American children begin to be immunized against tetanus and other diseases at a very early age. But instead of being exposed to the tetanus bacteria, the children are given shots containing a purified and chemically changed toxin. The new toxin is no longer poisonous but it still triggers the lymphocytes to release antibodies. After several injections, the lymphocyte cells retain a kind of "memory" and will release antibodies against tetanus bacteria for years to come. What is remarkable about this "immunological memory" is that it is rather exact. Tetanus shots protect us against tetanus, but not against polio or measles or any other disease. That's why children are given several different kinds of shots.

Government immunization programs had a strange beginning involving an eighteenth century English physician and a milkmaid. Jenner, the physician, had been concerned with smallpox for a quarter of a century before he performed a famous experiment which we will review shortly. Smallpox is a highly contagious virus disease characterized by fever, vomiting and numerous pustules (small elevations of the skin that are full of pus). This disease is rare now but once it was a dreaded killer--in one terrible year of the middle ages, more than one-quarter of the population of Europe was wiped out by smallpox. And in Jenner's day, more than thirty per cent of English children died because of smallpox. Jenner believed he knew how to prevent smallpox. He was aware of a few curious facts. Smallpox attacked fewer people on farms than in cities. However, farm workers often got cowpox, a disease that was like a very mild smallpox.

Jenner (and many others) believed that people who contracted cowpox became immune to smallpox. To test his idea, Jenner performed an extraordinary and ethically questionable experiment. When a young milkmaid with cowpox came to his office, besides examining her, he removed some fluid from one of her pustules and later injected the material into a healthy eight-year-old boy. A few months later he injected the boy with fluid from smallpox pustules! Fortunately, Jenner's theory was correct--the boy did not get smallpox. Soon after his experiment was reported England began using cowpox fluid to immunize school children against smallpox. The practice of immunization is now widespread--most countries have immunization programs.

Jenner did not know that smallpox was caused by a virus--viruses are much too small to be seen with the kinds of microscopes that were available in Jenner's time. He also didn't know how immunization worked. Can you suggest an explanation of how the boy in the story became immune to smallpox? Such an explanation should include reference to lymphocytes and antibodies.

What is the general function of white blood cells?

Do the different kinds of white blood cells perform this function in the same way? Explain.

How does a neutrophil destroy a pathogen?

Where does phagocytosis occur in the body?

What kind of white blood cell contributes to immunity? In what way?

What is meant by "immunological memory?"

What is injected to prevent tetanus?

Vocabulary:

antibody (AN-tih-BAHD-ee)--a blood protein (globulin) responsible for immunity; antibodies include antitoxin and opsonins.

immunity (ih-MEW-nih-tee)--the condition of being resistant to infection or disease.

immunology (IM-yoo-NOL-uh-jee)--the science dealing with antibodies and immunity.

lymphocyte (LIM-fo-site)--a kind of white blood cell that produces antibodies.

neutrophil (NEW-truh-fil)--a kind of white blood cell that is phagocytic.

opsonin (OP-suh-nin)--an antibody in blood plasma that prepares bacteria for phagocytosis.

phagocytosis (FAG-o-sy-TOE-sis)--the act of surrounding and digesting foreign bodies or particles by a cell.

pustule (PUS-tyool)--a small elevation of the skin containing pus.

smallpox--an infectious disease characterized by fever, vomiting and numerous pustules.

tetanus (TET-uh-nus)--an infectious disease characterized by stiffness of the body, muscle spasms and convulsions; sometimes called "lockjaw."

SECTION 15: IMMUNITY AND THE LYMPHATIC SYSTEM

15-1 An "Artificial" Immunity

What can be done when natural immunity develops too slowly?

In Section 14 we considered how a person becomes immune to infectious diseases. In the cases discussed so far, the immunity generally involved the following events.

1. The foreign body (antigen)* enters the body.
2. The antigen contacts a lymphocyte.
3. The lymphocyte makes antibodies that react with and destroy the antigen.

*The term "antigen" means a substance that stimulates antibody production. Antigens are also referred to as "foreign bodies" because they generally come from outside the body. Antigens are typically large molecules such as proteins. They may be toxins produced by bacteria (the corresponding antibodies being "antitoxins"). Antigens may be on the surface or inside a microbe. Sometimes the entire microbe is referred to as an antigen, but this is misleading--a microbe contains many different antigens.

Because these events require the lymphocyte to play an active role in making antibodies, this kind of body defense is called active immunity. It takes time to develop active immunity. Sometimes a series of shots over a period of months or years are needed to build up resistance against a disease by this process. And this time factor can result in problems. Suppose there were an outbreak of botulism, a kind of bacterial food poisoning discussed in the Nutrition Unit. The toxin produced in this kind of food poisoning is very powerful. It often causes paralysis and death within several days unless the victim can be quickly immunized. But active immunity is out of the question; the patient would almost certainly die before producing enough antibody to neutralize the toxin. However, if the disease is diagnosed early, there is another way to provide immunity. Can you guess what it is?

The answer is to inject the person with prepared antibodies that neutralize or counteract the toxin. Serum containing such antibodies is available in hospitals for emergencies. The "artificial" immunity provided by these antibodies is not long-lasting, but it can save lives. It is called passive immunity because the lymphocytes of the infected person are not actively involved in making the antibodies. (The antibodies may, for example, have been obtained from horses given a series of injections of modified toxin.)

15-2 Some Properties of Antibodies

How can antibodies handle all the different kinds of antigens?

The antibodies involved in both active and passive immunity have several important properties that deserve re-emphasis.

1. They are proteins.
2. They are specific for particular antigens.
3. They are made by lymphocytes.

If each antibody is specific for a particular antigen, then there must be an enormous number of different kinds of antibodies made by lymphocytes--because there are tens of thousands or more different antigens. (For example, each different kind of bacterium contains different antigens.) How can there be so many different antibodies?

The answer lies in the fact that antibodies are proteins. Recall that proteins are composed of some twenty different kinds of amino acids, and these amino acids can be arranged in numerous different ways. It has been shown that antibodies for different antigens have different amino acid compositions. By using different amino acids and arranging them in different sequences, the lymphocytes can make an enormous number of different antibodies. It is believed that each antibody protein can "recognize" and react with a different antigen in the same way that each different enzyme protein can "recognize" a different substrate molecule.

Since antibodies are proteins, you might expect that a significant increase or decrease in antibodies could be detected in the laboratory. As a matter of fact, such changes can be detected by electrophoresis. Most antibodies migrate with the gamma globulin fraction of plasma proteins. In Section 13 we considered a few diseases with characteristic electrophoretic patterns. One of these was chronic microbial infection. In this condition, the body tries to defend itself from pathogens by producing large amounts of antibodies. As a result, people with chronic infection have electrophoretic patterns with excessive gamma globulin. On the other hand, in hypogammaglobulinemia, the patients lack the ability to make enough antibodies. Their electrophoretic patterns are characterized by a small gamma globulin band.

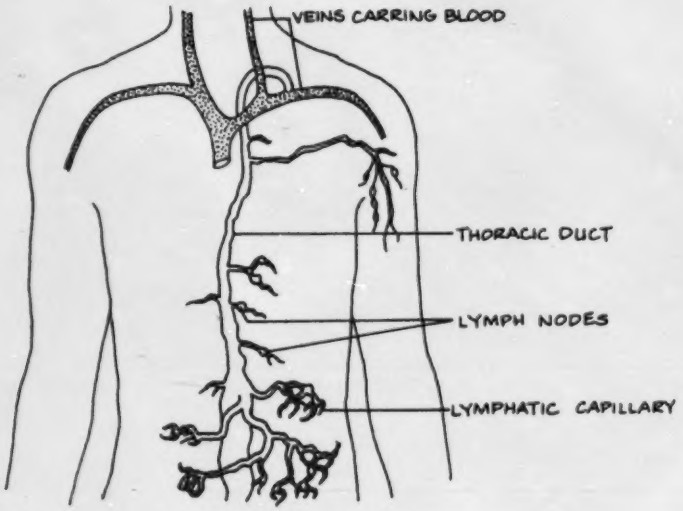
15-3 The Lymphatic System--A Secondary Circulatory System

What does the lymphatic system transport?

As the title of this section indicates, there really are two circulatory systems. So far we have been emphasizing the system that transports blood. There is also another system that circulates fluids through the body. It is the lymphatic system, and its fluid is not blood but lymph.

We have already mentioned the lymphatic system briefly in the Nutrition Unit. In Section 8 of that unit we indicated that most fats are absorbed directly into the bloodstream. Fats and fat-soluble vitamins (vitamins A and D) collect into tiny droplets which move through the body in the lymphatic system. In addition, this system is where much of our lymphocytes are made. So the lymphatic system is central to immunity.

In order to understand how the lymphatic system works, we will begin by studying its parts (see figure). The system is actually much more extensive than shown. Its vessels reach throughout the body. However, the part of the system shown in the figure is enough to allow us to consider how fluids circulate throughout the lymphatic system. Note that the lymphatic system has tubes (ducts) that look like veins, and it has capillaries. But it has no heart to pump fluids through the system. And the lymphatic capillaries differ from the capillaries that transport blood. A capillary that transports blood is open at both ends; one end connects with an arteriole and the other end connects with a venule. The lymphatic capillary has a closed end; it is like a tiny finger.



Interstitial fluid diffuses into the lymphatic capillaries. Once in the lymphatic vessels, the fluid is known as lymph. This fluid is like blood but contains fewer proteins and no real blood cells. Its color is whitish rather than red. The lymph flows from the capillaries into larger and larger vessels ending in large ducts as shown in the figure. Near the neck, a large lymph duct (the thoracic duct) connects with a vein and the lymph empties from the lymphatic system into the bloodstream. Here and there along the duct, there are small swellings called lymph nodes. The lymph nodes are where a large proportion of our lymphocytes are made.

What makes lymph flow? Unlike the circulatory system, the lymphatic system has no pump to force fluid through it. But the lumph vessels run along many body muscles. As these muscles contract during normal movements, pressure causes the lymph to move. One-way valves permit movement in only one direction. The movement is slow and irregular, unlike blood flow.

15-4 Another Function of the Lymphatic System

How does the lymphatic system help to prevent edema?

In Section 12 we considered how certain conditions led to the escape of fluid from blood vessels into the interstitial fluid and this process can result in edema. You may recall that fluids tend to move out of the capillaries at their arterial end and flow back into the capillaries at their venous end. However, the net flow outward (i.e., from the capillaries to the interstitial space) is greater than the flow in the opposite direction. But excess fluids, and especially the proteins that occasionally escape from the capillaries, have to be returned to the circulatory system or else very severe edema would result. Fortunately the lymphatic system serves this purpose. The lymphatic system returns about 2 to 4 liters of fluid to the body each day.

The normal distribution of proteins in the three body compartments (i.e., the circulatory systems, cells, interstitial space) is essential to the correct fluid balance in the body. The lymphatic system helps to compensate for the occasional leakage of proteins out of capillaries. Unlike the capillaries that carry blood, the lymphatic capillaries are much more permeable to proteins. So, any proteins that leak out from the blood vessels will tend to enter the lymphatic capillaries and eventually return to the blood.

How does passive immunity differ from active immunity? Give one advantage and one disadvantage of each kind of immunity.

How does the protein nature of antibodies explain the fact that there are so many different antibodies?

How would production of large amounts of antibodies affect an electrophoretic pattern?

What is the lymphatic system? What does it have to do with immunity?

How does the lymphatic system aid in maintaining a fluid balance in the compartments of the body? Why is this important?

Vocabulary:

active immunity--immunity that results from an individual producing his own antibodies.

antigen (AN-tih-jin)--a substance that stimulates the production of antibodies.

lymph (LIMF)--the fluid of the lymphatic system, collected from the interstitial space.

lymph node--a mass of tissue located in a lymphatic vessel.

passive immunity--immunity that results from an individual receiving antibodies made by another individual or organism.

SECTION 16: BLEEDING AND CLOTTING

16-1 Case History--The Bleeding Child

Alexis was an anemic three-year-old with a problem. He was a "bleeder" and he was bleeding now. Of course, all children have cuts and bruises and bleed from time to time, but Alexis was different. While most people stop bleeding from a minor wound in a few minutes, Alexis would sometimes bleed for hours. To say that his parents were concerned is an understatement. They were frantic. They feared that each bleeding episode might be the last for their weak child. They had talked to a number of physicians, but the doctors were unable to help since there was no cure for bleeders.

The bleeding continued and Alexis grew weaker. In desperation, his parents called on a man named Rasputin with a reputation as a healer. Rasputin stayed with the child for three days and three nights, praying all the time. Finally, the bleeding stopped. Alexis survived. The relieved parents thought that a miracle had been performed.

This is a true story. It happened in 1907, in Russia. Alexis was no ordinary child, nor were his mother and father ordinary parents. The parents were Nicholas and Alexandra, the Czar and Czarina, and they had immense power over the lives of millions. Their son, Alexis, was expected to become the Czar one day, for he was the only son among their five children. The royal family believed no sacrifice was too great to save their son. The Czarina became convinced that only Rasputin could keep her son alive and indeed, in several bleeding episodes, Rasputin could keep her son alive and indeed, in several bleeding episodes, Rasputin seemed to cure the child by magic. Rasputin, in turn, took advantage of his relation to the royal family and became one of the most powerful forces in Russia until 1916, when he was killed.

16-2 Why Does Bleeding Stop?

"Bleeders" like Alexis suffer from hemophilia, a disease that runs in families. The loss of blood in such people can lead to severe anemia, which explains why Alexis was so weak. The term "hemophilia" can be broken into two parts--"hemo-" (as in hemoglobin) meaning "blood" or, in this case, "bleeding" and "-philia" meaning "tendency toward." Hemophiliacs realize that any bleeding episode could be fatal. Minor accidents and especially internal bleeding are of real concern to the hemophiliac.

Why was it so hard for Alexis to stop bleeding? To answer this question, we might first consider a related question. Why do non-hemophiliacs stop bleeding so quickly? For example, bleeding from a small cut will normally stop in a matter of minutes. In those few minutes, the body responds in several ways to the wound. First, the blood vessels leading to the wound constrict (partially close). As a result, the leakage of blood through the opening slows down. Secondly, tiny structures in the plasma aggregate and stick together at the site of the opening. These structures are called platelets (Figure 1) and they are actually pieces that break off from larger cells. The larger cells that platelets come from are found in the bone marrow.

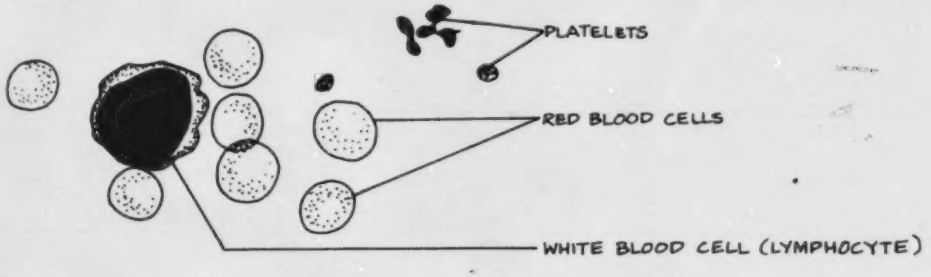


FIGURE 1: Platelets and blood cells.

In the case of a small wound, the platelets may actually stop the blood flow in a minute or two. (Remember that the blood vessels leading to the wound tend to constrict.) When this does not occur, the body weaves a fabric. This fabric consists of millions of microscopic fibers which we recognize as a blood clot. This clotting process normally takes only a few minutes. Then over a period of about 18 hours, the clot contracts and the serum is squeezed out. Thus, the clot becomes drier and harder and the edges of the wound are pulled closer together. All of these processes are part of healing.

16-3 How Does Blood Clot?

No doubt, you have seen many blood clots and perhaps have taken clotting for granted. If your blood was used for hemoglobin analysis or other Biomed activities, your blood has clotted within the last week or so. The importance of the clotting

process becomes more clear when the normal experience is contrasted with that of Alexis, for whom a slight accident could have meant death. Since the time of Alexis and Czar Nicholas II, we have come far in our understanding of blood clotting. The process is now known to be very complex, and there are still more questions to be answered.

We now recognize that the microscopic fibers of a blood clot are actually a protein, fibrin. And fibrin is an aggregation of many smaller protein subunits (see Figure 2).

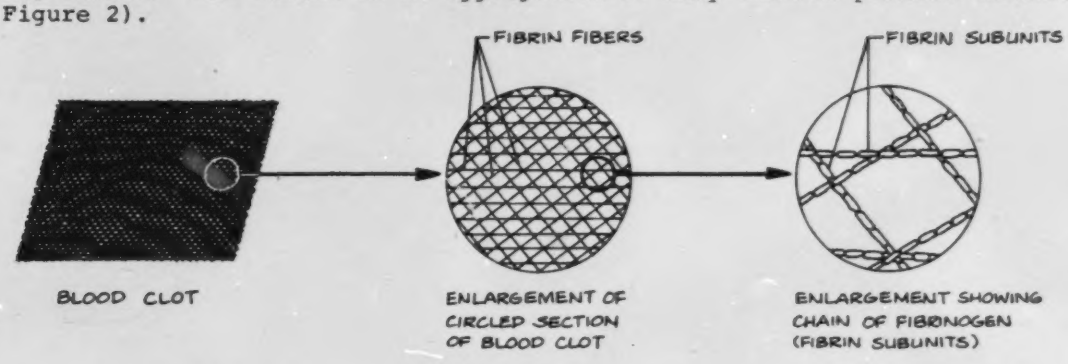

FIBRIN FIBERS
FIBRIN SUBUNITS
BLOOD CLOT
ENLARGEMENT OF CIRCLED SECTION OF BLOOD CLOT
ENLARGEMENT SHOWING CHAIN OF FIBRINOGEN (FIBRIN SUBUNITS)

FIGURE 2: A blood clot viewed at three different levels of magnification

You may wonder how the fibrin subunits come together to form a blood clot and how this process is related to hemophilia. For fibrin to form, a normal blood protein, fibrinogen, is required. Fibrinogen is converted into fibrin in the body. Fibrinogen will not form fibrin unless a special enzyme, thrombin, is present. For clotting to occur, an inactive protein, prothrombin, must first be converted to thrombin. These steps in clotting are summarized in Figure 3.

(1) Prothrombin ⟶ Thrombin

(2) Fibrinogen $\xrightarrow{\text{Thrombin}}$ Fibrin

(3) Fibrin ⟶ Blood clot

FIGURE 3: Three steps in blood clotting.

Blood clotting is, in reality, more involved than Figure 3 suggests. There are more than ten different factors required for blood to clot. Prothrombin and fibrinogen are two of the clotting factors. They are the only ones shown in Figure 3 because they are the factors most directly related to the actual clotting process. Yet if any of the ten factors are absent from an individual, that person will not be able to form clots normally. Most of the clotting factors are carried by the platelets, so these structures aid in clotting in two different ways: by aggregating and slowing up blood flow near the opening of a wound and by carrying the necessary clotting factors to the wound.

Alexis had a shortage of a protein, one of the clotting factors, needed to make thrombin. This is why he bled so long. Hemophiliacs such as Alexis will eventually stop bleeding in almost all instances. Because of the small amount of a particular clotting factor, it takes a very long time for enough thrombin to be made to permit the actual clotting. In view of this information, it is not at all surprising that Alexis stopped bleeding when Rasputin was around. Without Rasputin, he would have stopped bleeding too.

If Alexis lived now, instead of at the beginning of this century, he would receive periodic injections of blood extracts to provide him with the missing factor. In addition, special care would be given to avoid bleeding both externally and internally. For example, good dental care would be even more important for Alexis than for a non-hemophilic child.

It is fortunate that blood generally clots at the right time. If our blood continually clotted, our blood vessels would soon be blocked and we would die. You may recall that sometimes blood clots at the wrong time or wrong place; such clotting can lead to Stage 3 of atherosclerosis. You might wonder why blood clotting does not happen more often in blood vessels. It has been shown that blood clotting is triggered by a decreased flow rate and by such factors as blood coming into contact with tissues or air. These factors are just the things that happen when a person is wounded.

What is hemophilia? How does it differ from iron-deficiency anemia?

What are platelets? List two ways in which platelets aid in healing.

How does blood-vessel constriction contribute to healing?

What is the relationship between fibrinogen, fibrin, thrombin and a blood clot?

Vocabulary:

fibrin (FY-brin)--the aggregate of proteins that makes up the fibers of a blood clot.

fibrinogen (fy-BRIN-uh-jun)--a soluble plasma protein that is converted to fibrin during blood clotting.

hemophilia (HEE-mo-FIL-ee-uh)--a disease involving faulty blood clotting.

prothrombin--an inactive protein that is changed to thrombin just prior to blood clotting.

thrombin--an enzyme that catalyzes the conversion of fibrinogen to fibrin.

SECTION 17: pH and BUFFERS

17-1 Acids, Bases and Homeostasis

What does homeostasis have to do with the pH of blood plasma?

In Unit II, we defined homeostasis as the property of resisting change in the body. By now, this idea is probably very familiar because we have found homeostatic controls involved in maintaining many body functions--blood glucose level, the volume of fluids in the compartments of the body and body temperature, to name a few. In addition, our blood plasma pH is maintained by an important homeostatic system that was discussed in detail in Unit I and will be reconsidered shortly. Even though we constantly produce acids and bases in metabolism, and even though we often ingest foods that are acidic or basic, our arterial pH normally remains very close to 7.4 and our venous pH a trifle less.

17-2 Acids, Bases, pH--A Review

How much do you remember about pH?

Before considering the effective pH regulatory devices of the body, it may be useful for you to review the concept of pH and how it relates to acidity. The following quiz will help you find which areas you may need to review. The answers appear at the end of this section.

SELF-QUIZ

1. Suppose you prepared and labeled three solutions in the laboratory but the labels fell off. You know one solution is acetic acid, one is a dilute base and the third is distilled water. Given wide-range pH paper, explain how you would decide which bottle was which.

2. Suppose you are given two solutions. Solution A has a pH of 7.8 and Solution B a pH of 9.2. Which solution is more acidic? Are either or both solutions acids?

3. Suppose you are given two beakers of solution. Solution A has a pH of 6.0, solution B a pH of 5.0. What is the mathematical relationship of the $[H^+]$ in the two beakers? (In other words, is A six-fifths as acidic, or half, or a tenth as acidic as B?) Explain.

4. Suppose you are handed two test tubes. Tube A contains 0.1 M HCl (hydrochloric acid) and B contains 0.1 M $HC_2H_3O_2$ (acetic acid). Would the two tubes have the same pH? Explain.

5. Suppose you have a kid sister who drinks milk with a straw. One day she clowns around by blowing bubbles into her milk. You tell her to stop it because she is making her milk acidic. She doesn't believe you. Explain how you would try to convince her.

17-3 The Buffers of the Blood

How do buffers work?

In Activity 17, you added hydrochloric acid (HCl) to each of three solutions--water, sodium bicarbonate ($NaHCO_3$) solution and sodium chloride (NaCl) solution. Later you repeated the procedure using sodium hydroxide (NaOH), rather than HCl. In each case, you measured the effect of adding either acid or base on pH. You probably found that one of the three solutions (the $NaHCO_3$ solution) "resisted" change in pH--that it changed very slowly as acid or base was added. Substances such as sodium bicarbonate that resist a pH change are known as buffers. The buffers of the blood help to maintain pH. They are homeostatic controls.

Several different kinds of buffers are present in the blood. But all of them have the ability to neutralize acids or bases added to blood. Many buffers are combinations of weak acids and their salts. An example of this kind of buffer is a mixture of lactic acid and sodium lactate. Some blood buffers are proteins, and they are very important in pH control.

CO_2 dissolved in water provides one example of a blood buffer. CO_2 and H_2O can react to form carbonic acid (H_2CO_3). However, almost all of the carbonic acid formed either dissociates into H^+ and HCO_3^- or back into CO_2 and H_2O. Thus, although H_2CO_3 is a necessary intermediate compound, the important equilibrium in blood is

$$H_2O + CO_2 \rightleftharpoons H^+ + HCO_3^-$$

At equilibrium, the solution will contain mostly dissolved CO_2 plus a small proportion of H^+ and HCO_3^-.* How can Equation 1 explain the ability of this mixture to resist changes in pH?

Let's first consider the effect of addition of an acid such as HCl to a solution. When HCl is added to a solution, it ionizes almost completely into H^+ and Cl^-. The hydrogen ions cause the pH to drop. However, in the presence of a CO_2-bicarbonate mixture, the hydrogen ions added react with the HCO_3^- in the solution, and the equilibrium shifts to form more H_2O and CO_2. So most of the hydrogen ions added are removed from the solution and the pH does not drop significantly. In this way the CO_2-bicarbonate buffer in the blood resists a drop in pH due to production of acids (such as pyruvic acid) in metabolism.

Now, consider the effect of addition of a base such as NaOH to a solution. In this case the NaOH ionizes almost completely into Na^+ and OH^-. The hydroxide ions (OH^-) will cause the pH to increase. But in the presence of the CO_2-

*The CO_2, H^+ and HCO_3^- shown in Equation 1 are actually in equilibrium with other substances in blood plasma. However, these other reactions are much less important quantitatively. In other words, they have little effect on Equation 1 and we can ignore them in this discussion.

bicarbonate buffer, the OH^- added reacts with the H^+ shown in the equation to form H_2O. As hydrogen ions are removed, the equilibrium shifts--more CO_2 is converted to HCO_3^- and H^+. The overall effect is to remove the additional hydroxide ions from the solution. In this way, the buffer tends to resist a pH increase due to production of bases produced in metabolism.

Not only is bicarbonate buffer important in maintaining the pH of the blood, but other blood components such as phosphates contribute to buffering. Especially important are the more concentrated proteins of the blood such as hemoglobin and albumin. What's more, the buffer systems work together. Each buffer itself has its limits. But the H^+ and OH^- that result from metabolism may be neutralized by a variety of blood buffers.

17-4 Parting Thoughts on pH and Homeostasis

What devices do we have to regulate blood pH besides buffers?

To a major degree, the homeostatic control of blood pH depends on buffers. The buffers of the blood are quick to respond to the challenge provided by acids and bases released in metabolism. The combined buffer system of an average person is theoretically sufficient to insure survival after addition of a liter of 1 M HCl to the bloodstream. (The assumption is complete rapid mixing of the acid.) Nobody has been foolish enough to try this experiment but calculations have shown that this volume of acid would lower the pH to 7.0. The victim would experience severe acidosis but probably not death.*

Although buffers are essential to pH control, respiration represents an even more important line of homeostatic defense against pH change. The release of CO_2 is tied closely to the pH of blood. When CO_2 is released rapidly from the lungs, as in rapid deep breathing (hyperventilation), the pH of blood goes up. In fact, the natural homeostatic response to acidosis includes hyperventilation. For example, CO_2 (which forms H^+ and HCO_3^-) and lactic acid build up in the body after vigorous exercise. This tends to make the body more acidic. We compensate for this situation by hyperventilating. This releases lots of CO_2 and resists a decrease of pH.

We have still another homeostatic mechanism. The composition of urine changes when there is a change in the pH of blood. If blood pH remains acidic or basic for a time, the kidney will excrete a more acidic or a more basic urine as needed for compensation. This explains why kidney failure may be associated with alkalosis (i.e., a blood pH that is too high) and acidosis.

List at least two homeostatic devices used in the body for regulation of blood pH.

How does a bicarbonate buffer resist a pH decrease when acid is added? How does it resist a pH increase when base is added?

Some blood buffers are mixtures of weak acids and their salts. What other kind of molecule is an important buffer of the blood?

Vocabulary:

buffer--a substance that tends to resist a change in pH.

ANSWERS TO SELF-QUIZ:

1. You could place a drop of each solution on the pH paper. The acid would produce a color corresponding to a pH of less than 7. The base would give a pH over 7. The distilled water should give a pH of 7 (or a little less if it contains dissolved CO_2) because it is neutral (neither acidic nor basic). Acids have pH

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*Acidosis, a condition involving low blood pH, has been considered earlier. A temporary condition of acidosis may result from strenuous exercise because CO_2 and lactic acid accumulate. More lasting acidosis is associated with diabetes.

values below 7, bases have pH values over 7. (For a review, see Science Unit I, Sections 29 and 30; Mathematics Unit III, Section 14.)

2. Solution A is more acidic than B even though neither solution is an acid (since both solutions are above pH 7). Conversely, we could say B is a more basic solution than A. The relative acidity depends on the $[H^+]$. For example, a pH 8 solution has a $[H^+]$ of 10^{-8} M (i.e., 0.00000001). (For a review, see references for Problem 1.)

3. The $[H^+]$ of A is one-tenth of that in B. A pH of 6.0 corresponds to a $[H^+]$ of 10^{-6} M. For a pH of 5.0, $[H^+] = 10^{-5}$ M, and 10^{-6} is a tenth of 10^{-5}. (For a review, see Mathematics, Unit III, Section 14.)

4. No. The 0.1 M HCl has a lower pH than the 0.1 M $HC_2H_3O_2$. Recall that for a given concentration, a strong acid (HCl) gives a lower pH than a weak acid (acetic acid). At a concentration of 0.1 M, HCl is almost completely dissociated, while almost all of the acetic acid is in the undissociated form. (For a review, see Science Unit I, Sections 29 and 30; Unit II, Section 28; Mathematics Unit III, Section 14.)

5. Explain to her that the air she is blowing into the milk is enriched in CO_2 as a result of respiration. CO_2 reacts with water to form carbonic acid (H_2CO_3). For a review, see Science Unit I, Sections 29 to 31, and Unit II, Section 25.

Another approach would be simply to check the pH of the milk with pH paper before and after she blows bubbles in it.

REVIEW SET 18:

1. List at least three functions of blood in addition to transport of nutrients to cells and transport of wastes away from cells.

2. List three kinds of cells present in blood and their functions.

3. What is unusual about the shape and interior of a red blood cell?

4. How are blood smears used in medicine?

5. What are the three compartments that house the fluids of the body?

6. What is "edema?" What are some causes of edema?

7. In electrophoresis, what factors determine the direction and distance of migration of a substance?

8. How is electrophoresis used clinically?

9. Compare and contrast the following terms: antigen, antibody.

10. Relate "antitoxin" and "opsonin" to antibodies.

11. Compare and contrast "active" and "passive" immunity.

12. List at least two functions of the lymphatic system.

13. What happens to fibrinogen when blood clots?

14. How does the body stop bleeding?

15. How does the body maintain a fairly constant pH in the blood plasma?

16. List at least two blood buffers.

SECTION 19: THE KIDNEYS AND EXCRETION

19-1 The Kidneys and Urea

How do the kidneys help to purify the blood?

Deep inside our bodies, there are two organs that look like giant brown beans. They lie near the small of the back just behind the abdominal cavity. Each weighs about 200 g and is roughly the size of a fist. These organs are called the kidneys (Figure 1) and without them we could not live.

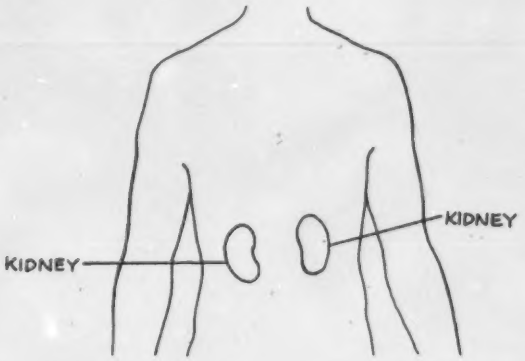


FIGURE 1: The position of the kidneys.

During metabolic processes in cells, small amounts of toxic compounds are formed as by-products. In small quantities, these compounds have little effect, but if they accumulate, they can reach a concentration that could cause bodily harm and even death. For example, if carbon dioxide were not continuously removed in respiration, acidosis and death would result. Ammonia (Figure 2) is one of the breakdown products of proteins and amino acids. If ammonia continues to build up, it can cause alkalosis and death. Fortunately, liver enzymes change ammonia to urea (Figure 2). Urea is a much less poisonous waste product than ammonia and causes no harm at normal concentrations. The urea goes from the liver through the bloodstream to all parts of the body. As the blood passes through the kidneys, these organs remove urea and other substances and eliminate them in the urine. This process, the removal of urea from the blood, is one of several homeostatic functions of the kidneys. These organs help to regulate the concentrations of a wide variety of chemicals in the blood. For example, as we discussed in the text on pH and buffers, the kidneys along with buffers and the respiratory system maintain the proper hydrogen ion concentration of the blood.

Ammonia (NH_3) Urea

FIGURE 2: Structural formulas for ammonia and urea.

19-2 The Liver and Purification of the Blood

How does the liver remove wastes from the blood?

The kidney, as we have seen, plays a key role in removing waste products from the bloodstream. But the liver also contributes to this important function. Blood flows from the intestines through the liver before entering the general circulation (Figure 3). Sometimes the blood entering the liver contains some bacteria and cellular debris. Phagocytes in the liver trap and break down bacteria and cell fragments. In addition, liver enzymes modify a number of toxic compounds to less poisonous or non-toxic forms, as in the conversion of ammonia to urea. Thus the liver

removes undesirable materials from circulation. In essence, it makes the task of the kidneys easier.

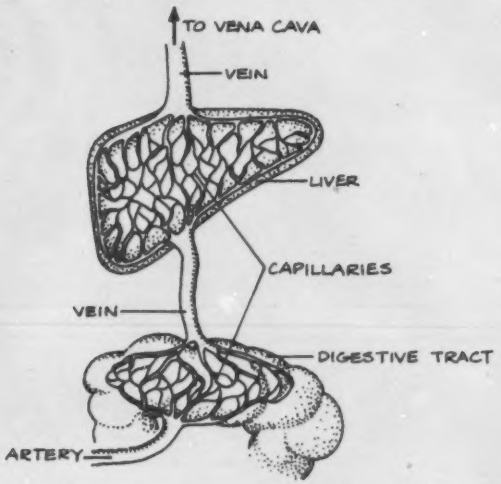


FIGURE 3: The route of blood from the intestines to the rest of the body via the liver.

19-3 The Kidneys and the Volume of Fluids in the Body

Aside from removing wastes and poisons from the blood, the kidneys also help to maintain the proper volume of fluids in the body. In Section 12, we discussed water balance in the three body compartments (i.e., cells, circulatory system and interstitial space). Without homeostatic controls that regulate the volume of fluids in each body compartment, serious health problems such as hypertension and edema result. Fortunately, the body has several ways to increase or decrease the volume of fluids in its compartments. Chief among these is the production and release of urine by the kidneys. Normally we eliminate one to two liters of urine per day, but this volume can be varied greatly in response to the needs of the body.

Let's look in on Parched Pete, a fellow who's always too busy to drink anything with lunch. He always gobbles down a sandwich and then rushes off so he can play badminton with Elmira Lagoon. Pete never worries about a decrease of water in his three body compartments. Little does Pete know, his brain automatically takes care of him.

Because he doesn't drink enough water, the salts in Pete's blood and in the interstitial fluid bathing all his cells tend to become more concentrated. This causes Pete's cells to shrink (Figure 4 reviews the reason).

Cell in Salty Solution

WHEN A CELL IS SURROUNDED BY A HIGHLY SALTY SOLUTION, IT SHRINKS BECAUSE OF THE FOLLOWING EVENTS. THE LIQUID INSIDE IT HAS A HIGHER CONCENTRATION OF WATER THAN THE SOLUTION AROUND IT. WATER DIFFUSES FROM WHERE IT IS IN HIGH CONCENTRATION (HIGH PERCENTAGE) TO THE REGION OF LOW CONCENTRATION, WHICH MEANS WATER DIFFUSES OUT OF THE CELL.

Cell in Dilute Solution

WHEN A CELL IS SURROUNDED BY A VERY DILUTE SOLUTION, IT SWELLS UP AND IT MAY EXPLODE UNDER PRESSURE. THIS HAPPENS BECAUSE WATER DIFFUSES FROM WHERE IT IS IN HIGH CONCENTRATION, OUTSIDE THE CELL, TO WHERE IT IS IN LOW CONCENTRATION, INSIDE THE CELL.

FIGURE 4: Review of osmosis.

When this happens to a group of cells in the hypothalamus (Figure 5), in the brain, Pete feels thirsty. He leaves Elmira on the badminton court and rushes off to the water fountain. He drinks and drinks and thus dilutes his salts back to the normal concentration.

Suppose Pete just can't bear to leave Elmira, and he ignores the signals from his hypothalamus. What will happen? If Pete still doesn't drink water the pituitary gland in his brain responds (Figure 5). This small gland, the size of a pea, releases a hormone that signals the kidneys to make less urine. It's called antidiuretic hormone. (Recall that a diuretic is a substance that increases urine flow. Hence the name "antidiuretic.")

How does the body react when you drink too much? Water from the excess fluid enters the blood. Fortunately, your kidneys take that excess water from the blood and automatically make it into more urine. In addition, the pituitary gland responds to this situation by making less antidiuretic hormone. The decreased level of this hormone reaching the kidneys also favors the production of more urine. So, whether you drink too much or too little, the kidneys maintain the correct volume of water, with a little help from the hypothalamus and pituitary gland.

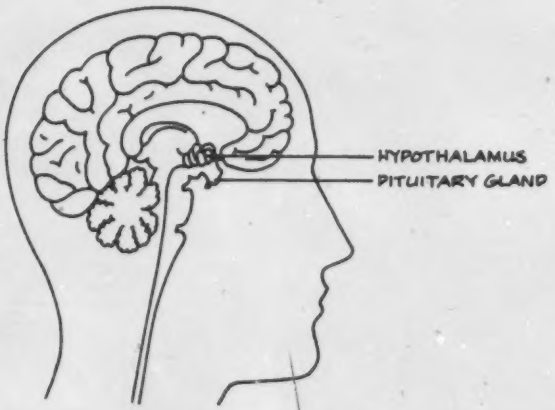


FIGURE 5: Location of the hypothalamus and pituitary gland in the brain of Parched Pete.

19-4 The Kidneys and the Excretory System

Why are the kidneys discussed in a unit on the circulatory system?

We have seen that the kidneys are involved in elimination of body wastes or excretion. They are, therefore, part of what is called the excretory system.* So you may wonder why we are discussing the kidneys in a unit on circulation. The reason is that the two systems are closely related. As we have already indicated, the kidneys help govern the quantities of chemicals in the circulatory system. And, of course, the fluids entering the kidneys come from the circulatory system. The heart pumps blood to all parts of the body via the circulatory system; the kidneys then maintain the quality of the blood being circulated so that we are not poisoned

*There is more to excretion than simply elimination of urine. For example, water and carbon dioxide may be considered as body wastes. They are excreted by the lungs as we exhale, so the lungs are part of the excretory system. In addition, the skin is considered part of this system because it releases water and salt in the form of sweat. Finally, the colon and liver may be included as components of the excretory system because they eliminate body wastes.

by the by-products of our own metabolism. Each day about 1,600 liters of blood flow through our kidneys and about one-thousandth of this volume becomes urine.

Where are the kidneys located? The pituitary gland?

How do the kidneys help to prevent poisoning of the body?

What other organ performs this function?

List as least two ways in which the kidneys contribute to homeostasis.

What happens to the amount of urine your kidneys make if you drink too much? If you don't drink enough?

How do the hypothalamus and pituitary gland help to regulate the amount of water in the body?

Vocabulary:

antidiuretic hormone (AN-tee-DY-yu-RET-ik)--a hormone produced by the pituitary gland that causes less urine to be made.

excretion (eks-KREE-shun)--the elimination of waste products.

excretory system (EKS-kruh-tor-ee)--the body system that functions to elminate waste products.

hypothalamus (HY-po-THAL-uh-mus)--the part of the brain that controls the sensation of thirst in addition to other functions.

kidneys--the organs of the excretory system that eliminate urea and other wastes, and regulate the concentration of water, salts and other substances in the blood.

pituitary gland (pih-TEW-ih-TARE-ee)--a gland in the brain that secretes anti-diuretic hormone and other hormones.

urea (yu-REE-uh)--a waste product made in the liver from ammonia.

SECTION 20: HOW THE KIDNEYS OPERATE

20-1 Urine Production--The General Process

Where do the circulatory system and urinary tract meet?

In Section 19 we discussed what the kidneys accomplish and why they are so important. Now we will consider how the kidneys accomplish their main function--how they remove substances from the bloodstream.

The general process of urine production will be reviewed with reference to Figure 1. Each day about 1600 liters of blood pass through the hard-working kidneys. The blood enters each kidney through an artery (labeled "A" in Figure 1). This artery then branches into arterioles. From these arterioles, the blood passes through capillaries into venules. The blood in the venules collects in a vein (B) which carries the blood from each kidney back to the heart.

But a lot happens to the blood as it moves from the arterioles to the venules of the kidneys.

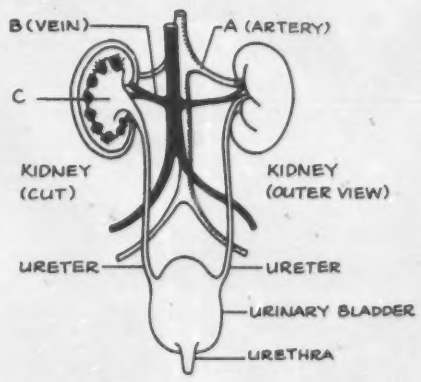


FIGURE 1: The urinary tract and related blood vessels.

The blood passes through an enormous length of tightly coiled capillaries. If laid out end to end, these capillaries would extend over 55 kilometers (about 35 miles). And as the blood passes through all this tubing, some of the water, ions and molecules it contains leaves the capillaries of the circulatory system and enters the urinary tract (Figure 1). The urinary tract consists of the kidneys, the ureters, the urinary bladder and the urethra. Urine collects in the hollow region of each kidney (C) and then enters thin, muscular tubes called ureters (one from each kidney). The ureters carry urine to the bladder, for temporary storage (Figure 1). The bladder is a hollow muscular organ. When the bladder is filled with several hundred ml of urine, nerve signals normally cause the bladder to empty. From the bladder, urine is eliminated through another tube, the urethra.

To hold their urine, adults voluntarily inhibit their bladder muscles. They also contract a ring of muscle (a sphincter) in the urethra, the tube that carries urine out of the body from the bladder. Infants, who have not yet learned to control the bladder and urethra muscles, urinate whenever the nerves signal the bladder to empty.

20-2 Urine Production--A More Detailed View

What happens to water and sodium ions in the tubules?

In order to understand the waste-removal process of the kidneys, anatomists have had to examine the kidneys in far more detail than shown in Figure 1. By careful dissection, they have found that each kidney has numerous tubes like the one circled in Figure 2A. These structures are actually complex networks of tubing as shown by Figure 2B. The web of tubing is called a nephron, and there are over a million nephrons in each kidney. Each nephron contributes to the production of urine.

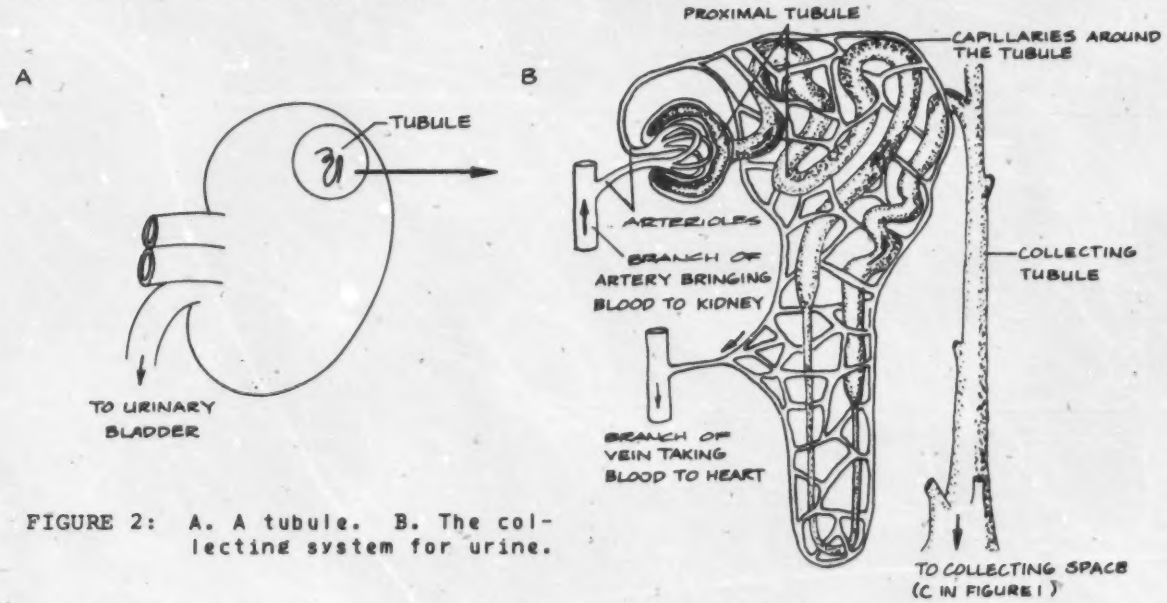


FIGURE 2: A. A tubule. B. The collecting system for urine.

As the blood flows through the capillaries (Figure 2B), water, salts, acids, urea and other compounds diffuse from the bloodstream where they are at relatively high concentrations into the kidney tubules. In fact, just about everything dissolved in blood plasma except proteins is small enough to diffuse through the capillary membranes.

Let's focus first on water, because maintaining the proper volume of water is one of the most important aspects of kidney function. Each day about 180 liters of water pass from the capillaries into the tubules. If all that water became urine (and was excreted), you'd have to drink 720 glasses of water daily to keep from drying up! Fortunately, over 99 per cent of the water that enters the tubules goes back into the bloodstream. Only about 1.5 liters of the 180 liters of water that enters the tubules is excreted as urine.

What about the rest of the water that enters the tubules--some 179 liters? In order to maintain the right balance of fluids in the body compartments, this water must get back into the bloodstream. It must be reabsorbed. The kidneys have a rather tricky device to accomplish this, and it involves Na^+ ions. First Na^+ ions are moved from inside the tubule to the surrounding interstitial space (Figure 3A,B).* They are caused to move by the cells that are in the walls of the tubule.

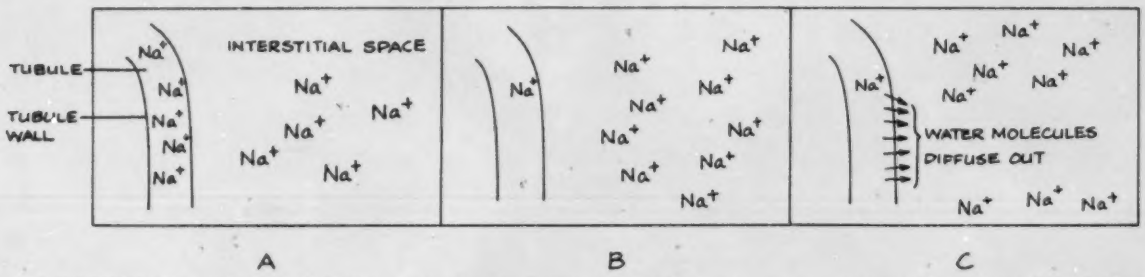


FIGURE 3: How osmotic pressure causes water to move into the interstitial space around the tubules. A. Na^+ is balanced inside and outside the tubules. B. Na^+ ions move out of the tubules into the surrounding interstitial space. Note that Na^+ ions continue to move into the interstitial space even after there is a higher concentration of Na^+ in the interstitial space than in the tubule. This results in osmotic pressure inside the tubules. C. Osmotic pressure causes water molecules to move out of the tubules.

The result of this movement of ions is to increase the Na^+ ion concentration in the interstitial space around the tubule. Then, because of osmotic pressure resulting from the Na^+ ion imbalance, water moves through the tubule walls into the interstitial space. The water moves from a region of higher concentration to one of lower concentration (Figure 3C). The concentration of water and Na^+ ions builds up in the interstitial space. From there, the Na^+ ions and water re-enter the capillaries (reabsorption) around the tubules and flow with the blood to venules and veins. By this process, the blood recaptures most of its water and Na^+ ions. About 75 per cent of the reabsorption of water occurs in the first part of the tubule. This region is called the proximal tubule (Figure 2). Other ions and nutrients are also reabsorbed.

20-3 The Movement of Sodium Ions Out of the Tubules: Active Transport

How can sodium ions move into a region of higher concentration?

Consider Figures 3A and 3B. There should be something disturbing about the migration of Na^+ ions. How can these ions move from a region of lower to one of a higher concentration? What happens is different from what we would predict from earlier discussions of diffusion.

The movement of ions is not due to diffusion, but rather to a process called active transport. The cells in the walls of the tubule must be "active" in this operation in order to force Na^+ ions against their usual direction of movement. Unlike normal diffusion which can occur in a test tube as well as in a living organism, active transport is one of the special properties of life. It is not limited to Na^+ ions or to kidneys, but involves many kinds of substances and occurs in all kinds of cells. And when a cell dies, active transport stops.

It is not known exactly how active transport works in all cases, but some of its features are understood. First, active transport appears to be carried out by enzyme-like proteins, called "carriers," which are found in cell membranes. Each type of carrier, like an enzyme, is highly specific for a particular substance. For example, there are carriers in the walls of kidney tubules specific for Na^+ ions. The carrier is thought to function by binding to a particular substance and helping it to pass through the cell membrane.

*This process is not simple diffusion. It is a special process which we will return to after we examine the general events of the process.

The second thing known is that active transport requires an input of cellular energy. ATP, which was considered in the Nutrition Unit, must be present for active transport to occur. This is known to be true because if we add to a cell a poison that interferes with cellular respiration (the process that produces ATP), active transport stops in that cell. It is believed that the cell uses energy from ATP in the process of building the carrier molecules, which in turn carry out active transport.

20-4 The Control of Salt Concentration in Body Fluids

How do the kidneys regulate the concentration of salts in our body fluids?

We have seen how important Na^+ ions are to the removal of water by the kidneys. It is important also to regulate the Na^+ ion concentration of blood, and the kidneys are involved in this form of homeostasis, too. The sodium ion concentration of plasma is normally around .135 to .145 moles per liter, and it doesn't vary much no matter how much salt is in the diet.

Let's look in for a moment on Sidney the Cell to see how Na^+ concentration is regulated. He lives in Parched Pete. Sidney is like an island--surround by interstitial fluid (Figure 4). Like all cells, Sidney is finicky. It's important for him to have just the right concentration of Na^+ ions in the interstitial fluid around him. If there are too many Na^+ ions around him, he'll shrink, and if there are too few, he'll swell up and possibly burst.

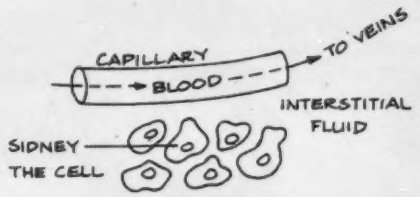


FIGURE 4: Sidney the Cell and his environment.

Parched Pete is really involved in his badminton games with Elmira Lagoon and pays little attention to his diet. He apparently is not worried about the relation between high-salt diets and hypertension--he loves pretzels and potato chips. On his birthday, his sister gave him two pounds of salty pretzels which he shared with Elmira--1.9 pounds for Parched and 0.1 pounds for Elmira.

All that salt led to a predicament for Sidney the Cell. The Na^+ ion concentration in the blood in nearby capillaries and in the interstitial fluid began to increase. Parched Pete's kidneys began to work. They removed the extra Na^+ ions (and Cl^- ions) from the blood and excreted them with the urine. As the salt concentration in the blood in nearby vessels decreased, Na^+ ions and Cl^- ions began to move back into the blood from the interstitial fluid. Soon the ion concentrations in the interstitial fluid surrounding Sidney decreased back to the normal range, even though Pete had eaten so much salt.

How did Pete's kidneys get rid of all the extra Na^+? The kidneys have special Na^+-detector cells near the tubules. When there is very little Na^+ in the interstitial fluid surrounding these detector cells, they make a substance that stimulates the nearby adrenal glands (Figure 5) to make and secrete a hormone called aldosterone. Aldosterone causes the tubules to transport more Na^+ to the surrounding interstitial space and thus to the bloodstream. When the amount of Na^+ in body fluids increases, the Na^+-detector cells cause the adrenal glands to make less aldosterone. As a result, less Na^+ is transported out of the tubules, and therefore more Na^+ leaves through the excretory system. Pete's kidneys solved his pretzel problem for him by signalling his adrenal glands to secrete less aldosterone.

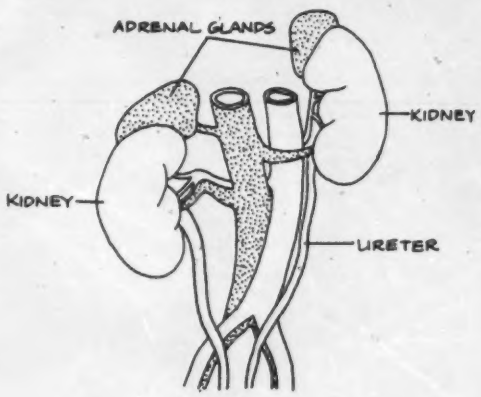


FIGURE 5: Location of the adrenal glands.

Periodically we have referred to hypertension and the current belief that too much dietary salt is in some way associated with this condition. In this section we have considered how the body regulates sodium-ion

concentration. It would be nice if we could now explain the exact relationship between sodium in the diet and hypertension. You might suspect, for example, that a high-salt diet leads to more sodium being reabsorbed by the blood vessels and, as a result, to more reabsorption of water into the bloodstream. If this were true, then the increased blood volume would explain how high blood pressure could result from a high-salt diet. Unfortunately, the evidence is that this is not true and the mechanism by which a high-salt diet may lead to hypertension remains to be discovered.

In what organs do substances pass from the circulatory system into the urinary tract? What kinds of vessels of the urinary tract are most directly involved in this transfer of materials?

What components of the blood leave the blood in the kidneys? What important component does not? Why not?

Of the water that leaves the blood, what percentage actually becomes urine? What happens to the rest of it?

How do Na ions aid in reabsorption of water?

Compare and contrast active transport and diffusion.

How is ATP involved in active transport?

Show the relation between the following terms: Na concentration, Na detector cells, adrenal glands, aldosterone, urine.

Vocabulary:

active transport--the movement of a substance from an area of low concentration to one of higher concentration (the opposite direction from diffusion).

adrenal gland (uh-DREE-nul)--a gland, lying on each kidney, that makes aldosterone and certain other hormones.

aldosterone (al-DAHS-tuh-rone)--a hormone that triggers increased active transport of Na^+ from the tubules; this decreases the amount of Na^+ excreted in urine.

nephron (NEF-ron)--a tubule together with many capillaries. There are about 1.5 million nephrons in each kidney.

proximal tubule (PROK-sih-mul)--the first segment of a kidney tubule.

tubule (TOO-byool)--a tiny, twisting tube in the kidneys which reabsorbs into the blood some substances but not others.

ureter (yoo-REE-tur)--a long, narrow tube that carries urine from the kidneys to the urinary bladder.

urethra (yoo-REE-thruh)--the canal through which urine is eliminated from the body.

urinary bladder--the organ that stores urine.

urinary tract--the passage for urine including the kidneys, ureters, urinary bladder and urethra.

SECTION 21: URINALYSIS

21-1 Urine in the Laboratory

What substances in the urine increase in diabetes? What else can analysis of urine reveal?

In Activity 20, you analyzed your own urine to see how a special diet affected its composition. This kind of laboratory study is called urinalysis (urine + analysis) and is a very important part of clinical medicine. Medical technologists are frequently given samples of urine to analyze for sugar or protein or other substances.

The data are then used by physicians to diagnose disorders such as diabetes and kidney diseases.

The belief that urine provides useful clinical information is a very ancient one. Physicians in ancient Greece, Rome, India and China attempted to diagnose diseases by inspection of urine. It is not clear that urinalysis was of genuine value in ancient times, but it certainly plays an important role in modern medicine. Medical technologists routinely make the following eight tests on urine specimens.

1. Blood and solid matter: First the urine is placed in a tube and centrifuged so that all solid matter, such as blood cells and kidney cells, are driven to the bottom. Bleeding in the kidneys and urinary tract can be detected by blood cells in the sediment at the bottom.

2. White blood cells: Urine is sometimes analyzed for the presence of white blood cells. If these are present, they may indicate an infection in the urinary tract.

3. Bacteria: Stains are used to see whether there are any bacteria. Their presence could mean infection. If bacteria are found in urine, they may be cultured on agar and identified biochemically.

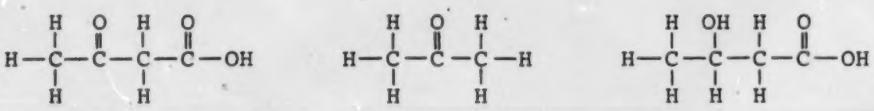
4. Excess protein: There is normally a little protein lost in urine, but too much can mean kidney disease.

5. Specific gravity: You may recall from Unit I that specific gravity is the ratio of the density of a substance to the maximum density of water. Normally the urine is denser than pure water; its specific gravity is 1.005 to 1.030. But the density can increase if excessive protein is being lost in the urine. On the other hand, it can decrease if a person drinks a lot of water or if the kidney is severely diseased so that it can't make a concentrated urine.

6. Glucose: People with untreated diabetes typically have high blood glucose (hyperglycemia). In such cases, this sugar passes into the kidney tubules in large quantities and builds up in them. When so much sugar builds up that it cannot all be reabsorbed back into the blood, some of it ends up in the urine. By testing their urine, diabetics can thus tell whether their blood-glucose concentration is getting too high. The analysis will tell whether the plasma glucose has reached a concentration of 200 mg/100 ml or more, for that is when glucose begins to show up in the urine. The normal plasma glucose level is 80 to 120 mg/100 ml. Glucose can also appear in the urine of normal persons after intake of a large quantity of sugar so that glucose in urine does not necessarily suggest diabetes.

7. pH: The pH of urine normally ranges from 5 to 8, depending upon the diet. A variety of conditions including diabetes may lead to a pH outside this range.

8. Ketone bodies: Some diabetics can't utilize glucose properly, so they tend to break down fats more than sugars for energy. Ketone bodies refer to three substances formed as a by-product of fat metabolism (Figure 1).



acetoacetic acid acetone hydroxybutyric acid

FIGURE 1: Structural formulas of the ketone bodies.

They are called "ketone bodies" because they either contain a "keto" group (-C(=O)-) or are made from other substances which contain such groups. Ketone bodies are normally excreted in small amounts, because some fat is normally used to provide energy (produce ATP). An increase of ketone bodies in urine, however, may indicate diabetes. Ketone bodies are also elevated in the blood in such cases.

Less common than the preceding tests is one for urobilinogen. This is the substance that gives urine its yellow color. Urobilinogen is made by bacteria in the

intestine out of a component of bile. It is absorbed into the blood and passes into the urine. Since it is derived from bile, some liver diseases lead to a decrease in the concentration of urobilinogen in urine.

21-2 Laboratory Tests on the Kidneys

What device is used to study the kidney directly?

Urinalysis provides much valuable information about how well the kidneys are performing. Yet there are times when it is important to study the kidneys directly rather than analyzing their product (urine). There are some ingenious methods to do this.

One such method for examining the kidneys involves a device known as a catheter (Figure 2). A catheter is a narrow hollow tube which can be introduced into the urinary tract or other body tubes such as blood vessels. The use of catheters in medicine has a long history tracing back at least to Ancient Greece and Rome some 2000 years ago. Antique catheters have been found made of bronze, copper, silver and even wood and leather. Insertion of catheters made of these materials must have been very painful. Catheters are inserted into the urinary tract from the outside. Modern catheters are made of materials that can bend. Such instruments have existed for about two centuries. Benjamin Franklin described an early flexible catheter in a letter he wrote to his brother in 1752.

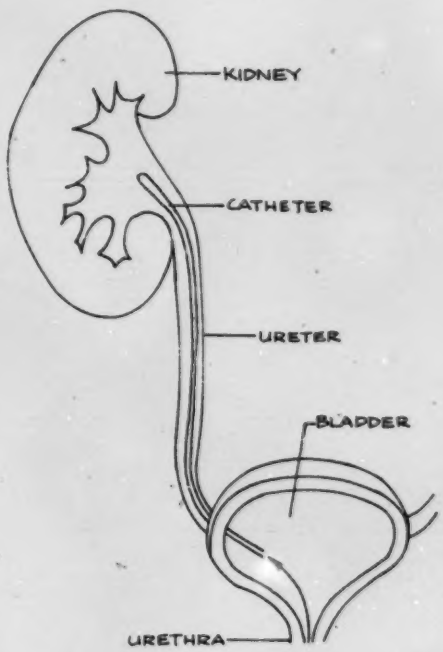


FIGURE 2: A catheter.

Until this century, catheters were used mainly to provide an exit for urine through an obstructed urinary tract, and they still are used in this way. (Obstructions may be caused by tumors and kidney stones.) But the development of finer, more flexible catheters, in addition to new laboratory techniques for analysis of very small quantities of urine, has increased the value of this device. For example, if a patient has a kidney disease, analysis of urine obtained with a catheter can establish whether the disease affects the left or right kidney or both kidneys.

The cystoscope is an instrument sometimes used to study the urinary tract. At first glance, it looks a little like a catheter. Both are long hollow tubes, but cystoscopes have lenses inside and a very small light bulb at one end. One application of the cystoscope is to peer inside the urinary tract of a living person. This technique is valuable because it may avoid unnecessary surgery. In addition to their use for viewing the urinary tract, cystoscopes have been modified to destroy tumors (cancerous cells) and to remove stones and debris from the urinary tract.

What is urinalysis? List some tests performed on urine.

What disease is sometimes indicated by ketone bodies in the urine? What other urine test is used to check for this disease?

What is a catheter? How is it used to study the kidneys? How is it used in treatment of urinary-tract disorders?

How is a cystoscope used in medicine?

Vocabulary:

catheter (KATH-uh-tur)--a flexible, hollow tube designed for insertion through a canal such as the urinary tract or a blood vessel.

cystoscope (SIS-tuh-scope)--a hollow tube with a light bulb at its tip, and containing lenses. It is used for viewing the interior of the urinary tract.

ketone body (KEE-tone)--a group name for one or more of the following compounds: hydroxybutyric acid, acetoacetic acid and acetone. Excess ketone bodies in urine is often an indicator of diabetes.

urinalysis (YOOR-uh-NAL-uh-sus)--examination of urine involving chemical, physical and microscopic tests.

SECTION 22: THE ARTIFICIAL KIDNEY AND KIDNEY TRANSPLANTS

22-1 The Artificial Kidney

When are artificial kidneys used?

Several situations can cause the kidneys to function poorly (kidney failure). Shock (to be discussed shortly) results from a decrease of blood pressure which in turn may lead to insufficient blood flow to nourish the kidneys. Heart attack can do the same thing. Carbon tetrachloride and other poisons may temporarily damage the tubules. When the kidneys fail, substances that are normally excreted in the urine are instead retained in the body. This condition is called uremia. (The suffix "-emia" means "blood," so the word "uremia" is derived from "urine in the blood.")

In uremia, substances build up in the body in dangerous amounts. For example, too much water is retained, and this raises the blood pressure. Also urea is retained, and urea is considered very slightly toxic. Of more importance is the retention of K^+ ions, for the heart is very sensitive to their concentration; too high a concentration of K^+ may cause the heart to beat irregularly or even stop. Recall also that the kidneys are important to the regulation of blood pH. In uremia, there is a tendency for acids to accumulate in the blood (acidosis). Table 1 compares normal blood plasma and plasma from a uremic individual ("uremic plasma").

TABLE 1: CONCENTRATION OF SELECTED SUBSTANCES IN NORMAL AND UREMIC PLASMA

	Normal Plasma (mg/100 ml)	Uremic Plasma (mg/100 ml)
K^+	20	30
Cl^-	380	415
HCO_3^-	165	85
uric acid	4	8
urea	25	200

When the kidneys function poorly, an artificial kidney may be used. The device was first used on animals in 1913, but it wasn't until the 1940's that it received its first use in humans. At that time it was used to compensate for kidney failure caused by battle wounds in World War II.

A major problem in uremia is to rid the blood of substances that are in dangerous concentrations. To do this, blood is made to trickle through narrow channels along a plastic semipermeable membrane. This membrane permits diffusion of substances from the blood to the other side of the membrane. The fluid on the other side of the membrane is called dialyzing fluid. (Dialysis refers to a diffusion technique used to control the concentrations of substances in blood. The technique is also used to separate and isolate substances from a mixture.) By adjusting the concentrations of substances in the dialyzing fluid, it is possible to increase or decrease the concentrations of these substances in the blood.

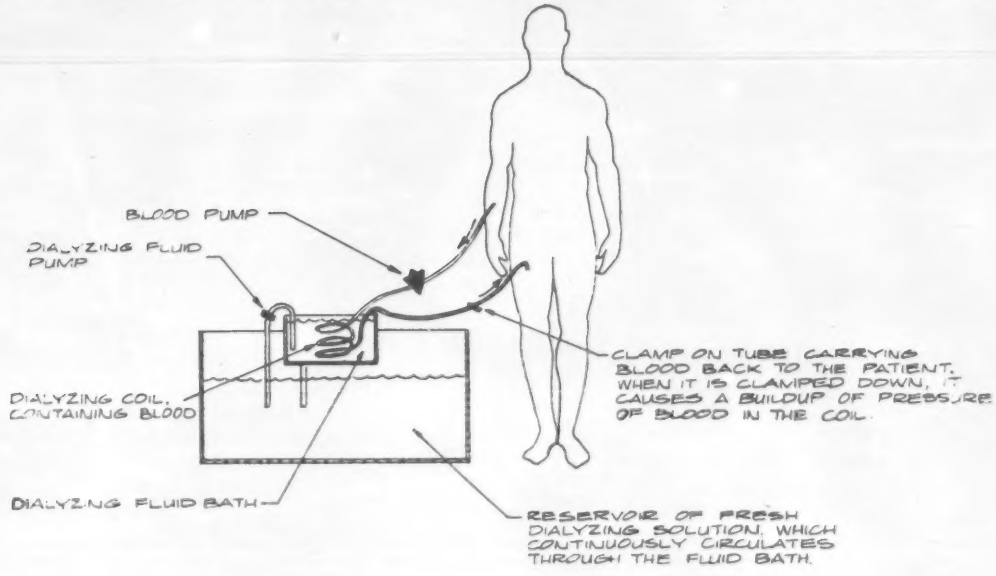
22-2 Dialysis in Detail

How does a dialysis machine work?

In cases of uremia, it is desirable to decrease the blood concentrations of K^+, urea and uric acid. The problems with accumulation of K^+ and urea have already been discussed. What about uric acid? Uric acid is a metabolic breakdown product of some nitrogen compounds obtained from the diet. This acid must be removed not because it is toxic, but because it is relatively insoluble. At high concentrations, uric acid tends to precipitate out in body joints--a condition known as gout. So one problem in dialysis is to remove materials from the bloodstream.

On the other hand, in uremia there are substances that need to be added to the blood, such as the important buffer bicarbonate. To do this, the dialyzing fluid is made up with a higher concentration of bicarbonate than that of the blood, so that HCO_3^- diffuses into the blood.

The plastic membrane must have pores small enough to keep cells and proteins from leaving the blood, but large enough to allow urea and other small molecules and ions to pass through. The figure below is a schematic drawing of a dialysis machine.


BLOOD PUMP
DIALYZING FLUID PUMP
DIALYZING COIL, CONTAINING BLOOD
DIALYZING FLUID BATH
CLAMP ON TUBE CARRYING BLOOD BACK TO THE PATIENT. WHEN IT IS CLAMPED DOWN, IT CAUSES A BUILDUP OF PRESSURE OF BLOOD IN THE COIL.
RESERVOIR OF FRESH DIALYZING SOLUTION, WHICH CONTINUOUSLY CIRCULATES THROUGH THE FLUID BATH.

A schematic drawing of a dialysis machine.

Normal kidneys work continuously, so people whose kidneys function poorly must spend many hours hooked up to the dialysis machine. They are usually treated three times a week, for four to six hours each time. A continuous hook-up is not needed because the dialysis machine removes urea, acids and K^+ ions from the blood faster than normally functioning kidneys. The concentration of urea in the dialyzing fluid is kept well below that in the blood. Other substances, such as potassium ions, have to be removed slowly, because too rapid a fall in the concentration would endanger the heart. So the concentration of these substances in the dialyzing fluid is maintained only slightly below the blood concentrations. To remove water, blood in the dialysis coil is put under pressure. Consequently, water is forced out through the membrane. This is done by manipulating the clamp on the tube which carries blood from the machine to the patient (see figure).

Dialysis is extremely costly when done at home with a dialysis machine and even more expensive when performed in a hospital. And although facilities have become more common, there may not be enough facilities to treat everyone who needs it, so decisions must be made about who gets treated. Those with the best chance of survival are likely to be given priority. If chances for survival are equal, age is often considered, younger people being given preference. Sometimes the decision is by random choice. Deciding "who shall live and who shall die" is a difficult question of

values, and different hospitals use different selection procedures. Recall the similar problems in the artificial heart activity considered in the social science course.

22-3 Kidney Transplants

What major problem must be overcome for a kidney transplant to succeed?

Dialysis is frequently used as a temporary measure by patients waiting for a kidney transplant. The chief problem is locating a kidney that will not be destroyed (rejected) by the patient's immune system. As we have considered, cells and antibodies of the immune system destroy invaders such as bacteria and viruses. A transplanted organ, such as a kidney, may be attacked as an invader. This is also true with heart transplants. The cornea of the eye, however, is not rejected when transplanted; it is not possible for antibodies and phagocytes to reach it.

Tissue typing, which is similar to blood typing, is done to find a kidney immunologically similar to the patient's. It can take months or even years for a donor with an appropriate kidney to turn up. ("Identical" twins don't have this problem because their kidneys are identical and are not rejected.)

Table 2 shows that kidneys transplanted from closely related family members are rejected much less frequently than those from non-relatives, so the closer the family relation between donor and patient, the better the chance for a successful transplant.

TABLE 2: PERCENTAGE OF TRANSPLANTED KIDNEYS STILL FUNCTIONING TWO YEARS AFTER THE TRANSPLANT

Donor	
Sister or Brother	81%
Parent	73%
Non-relative	40%

Even if a transplanted kidney is a good immunological match, there is still danger of rejection of the new kidney. To help prevent rejection, drugs that slow down antibody production must also be used. The most important ones are called "steroids." They resemble hormones made by the adrenal glands, and act by suppressing the patient's lymphocytes. (Recall that lymphocytes are the cells of the immune system which produce antibodies.) However, when steroid hormones suppress the lymphocytes, susceptibility to infections increases. Thus, even though the kidney may be accepted by a patient, the patient may die because of infection. The incidence of cancer is also higher among people taking steroid drugs. In spite of these problems, transplanting kidneys is an accepted part of modern medicine. Over 5000 kidneys have been transplanted throughout the world.

22-4 Shock

What causes shock?

As stated in Section 22-1, kidney damage often results from the medical condition of shock. This condition may be defined as a serious reduction of blood pressure. If shock continues for several hours, its effects are no longer reversible--the patient cannot be saved. For this reason, first-aid manuals direct the reader to watch for signs of shock in a wide variety of situations.

Remember Mr. Samuels, the man who had a heart attack (Section 6). After the heart attack, his blood pressure dropped to 90/50. Dr. Gardner who supervised the emergency-room treatment was also concerned about shock. It was obvious to him that Mr. Samuels was in shock--the patient was restless and anxious, his pulse was weak and he was sweating. Unfortunately, there was little to be done immediately except to administer oxygen.

Myocardial infarction is only one of several events that may lead to shock. Shock may occur because of a significant loss of body fluid. Heavy bleeding after a severe accident often results in shock. Shock may also follow loss of interstitial fluid (for example, from a bad burn), excessive sweating and even diarrhea.

Whatever the cause of the loss of body fluid, the result is a decrease in blood volume and consequently blood pressure. The decreased blood pressure results in less blood reaching vital organs such as the kidney.

Shock may be unrelated to loss of body fluids. You no doubt have heard instances of people fainting because of strong emotions. In such cases, the emotional event causes the dilation of arterioles and thus a decrease in arterial pressure. In turn, the decreased flow of blood to the brain causes the fainting. However, this kind of shock is usually mild and temporary and has no long-lasting effect.

What kinds of situations may cause uremia?

What substances accumulate in the body when uremia occurs? What bad effects does this have?

How does the artificial kidney extract accumulated substances from blood?

What important substance does the artificial kidney add to blood?

What is the major problem in successfully transplanting organs?

Why are kidneys from family members transplanted more successfully than kidneys from non-family members?

What are some dangers associated with the drugs used to help prevent kidney rejection?

What are some causes of the medical condition known as shock?

Vocabulary:

dialysis (dy-AL-ih-sis)--a diffusion technique used to regulate the concentrations of substances in blood.

dialyzing fluid (DY-uh-LY-zing)--the prepared solution in an artificial kidney, on the opposite side of the membrane from the blood.

gout--a condition involving the accumulation of uric acid in the joints of the body. Most often, the joints of the big toes are involved.

shock--a circulatory defect characterized by low blood pressure.

tissue typing--matching tissues of a donor with tissues of a recipient in locating an organ for transplanting.

uremia (yu-REE-me-uh)--accumulation in the blood of substances ordinarily eliminated in the urine.

SECTION 23: DISORDERS OF THE URINARY TRACT

23-1 Infections of the Urinary Tract

How do infections begin in the urinary tract?

Kidneys do not become diseased as often as the urethra and the urinary bladder. For an infection to begin in the kidneys, bladder or urethra, bacteria must either gain entrance from the outside and go up the urethra, or enter through the bloodstream.

Infections in the urethra are far more common in females than males. They are also common in people who have sexual relations with many partners and in untreated diabetics (sugary urine encourages bacterial growth). People with infections of the urethra find it painful to urinate, and feel like urinating more often than usual. If the bladder is infected, the symptoms are similar, but there is also pain transmitted from the bladder to the region of the lower abdomen. Chills and fever often

accompany these infections. It is important to treat these infections promptly, because they can spread upstream to the ureters and the kidneys.

Infections of organs of the urinary tract are treated with two types of drugs: antibiotics, such as penicillin and tetracycline, and sulfa drugs. It is important that treatment be thorough even though in many people symptoms disappear within a few days even without treatment. If treatment is not continued for a long enough period of time, a small number of bacteria may survive. The surviving bacteria may suddenly multiply at any time causing a recurrence of the infection. This explains why many people suffer from periodic urinary tract infections.

23-2 Kidney Disease

What are some of the major types of kidney disease?

Pyelonephritis is an important disease of the kidneys resulting from the effects of a current or past bacterial infection of that organ. In other words, pyelonephritis is not a bacterial infection, but rather a condition that results from an infection. A person may have a severe case of pyelonephritis with no bacteria demonstrable on urinalysis.

Pyelonephritis may involve any portion of the kidney. It is characterized by inflammation which, if chronic, may damage the tissues of the kidney. Many years may pass before kidney function is impaired to such a degree that symptoms of this disease are noted. When this does happen, a decrease in the kidney's ability to concentrate urine becomes evident. Hypertension is another common result of chronic pyelonephritis.

Acute pyelonephritis is almost always accompanied by a bacterial infection which results in fever and pain in the back in the region of the kidneys. The bladder is also often infected. Bladder infection occurs because urine containing bacteria from the infected kidneys travels to the bladder. In such cases, urinalysis will reveal bacteria and white blood cells.

Another disease of interest is polycystic kidney disease in which kidney tissue is replaced by spheres filled with fluid, called cysts (see Figure 1). (Note: These cysts are very different from the cysts we spoke of in Unit II in connection with parasites that infest the digestive tract.) This condition is hereditary. Most people don't discover it until they are at least forty years old. Then their kidneys continue to function, but deteriorate over a period of ten to twenty years.

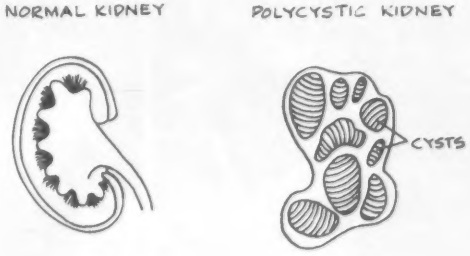


FIGURE 1: Interior view of normal and polycystic kidneys.

Glomerulonephritis, or inflammation of the glomeruli of the kidney, is another common disease of this organ. Glomerulonephritis often occurs a week or two after certain types of bacterial infections. In response to the bacterial invasion, the lymphocytes make antibodies. The antibodies attack the antigens of the bacteria, and antigen-antibody combinations form. These combinations circulate in the blood and are filtered out in the glomeruli of the kidney. (A glomerulus is a ball of coiled capillaries in a nephron.) The build-up of these antibody-antigen combinations in the glomeruli causes congestion and inflammation. It is this inflammation of the glomeruli that results in some of the symptoms characteristic of glomerulonephritis.

One common symptom of glomerulonephritis is the presence of protein and blood cells in the urine. This is a result of the increased permeability of the inflamed glomeruli. The congestion in the glomeruli also causes a reduced rate of urine production. In fact, fluid may actually back up in the kidney and the blood vessels. When this happens, liquid may seep out of the blood vessels and collect in the interstitial spaces of certain tissues, causing edema. Edema around the eyes and/or in the legs is a common symptom of this as well as other forms of kidney disease.

Other things also happen during the acute stage of glomerulonephritis. The urine may become cola-colored or blood-colored due to leakage of blood cells into

the urine. Upon microscopic examination, these blood cells are often seen embedded in masses of aggregated protein which has precipitated out of the urine and formed structures known as "casts." These casts are another result of decreased urine production. Casts are commonly seen in many forms of kidney disease.

Glomerulonephritis occurs in two main forms: acute and chronic. The acute form lasts only weeks or a few months. About 70 per cent of people who get it are under 21 and most recover completely. An artificial kidney may sometimes have to be used to tide the person over during a temporary period of no urine output.

Chronic glomerulonephritis is less common than the acute form, but it is more serious. It lasts for years and often ends in kidney failure, necessitating the permanent use of an artificial kidney or a kidney transplant.

An even more common ailment than glomerulonephritis is kidney stones. The stones vary in size from tiny particles, like sand, to large ones that fill the hollow portion of the kidney (the collecting area). Some have large projections sticking out like horns. These are called "staghorn" types (see Figure 2).

FIGURE 2: Outline of a typical staghorn stone.

Stones may form when various substances dissolved in urine (usually calcium salts) precipitate out in the kidneys. In most cases it isn't known why this happens. However, it has been suggested that chronic infection may be the cause. Another possible cause may be a high concentration of salts in the urine. A low urine volume also enhances precipitation, which is one reason that stones are more common in hot climates. People in hot climates do not produce much urine because they excrete most of their water in their sweat.

Small kidney stones can pass through the ureters and urethra and be eliminated in the urine. Passage of stones through the ureter and urethra causes agonizing pains. The pain begins when the walls of the ureter clamp down hard to move the stone along--a movement similar to peristalsis in the digestive tract. If a stone is too large, it may become lodged in the ureter. Sometimes, urine will back up behind the stone, putting pressure on the kidney and causing tissue damage.

It is important to realize that a large percentage of the kidney may be nonfunctional--about 85 per cent--before the patient is aware that anything is wrong. The same applies to liver function and to lung function, and it often takes years for this degree of impairment to occur in any of these organs. Urinalysis can show whether the kidneys are diseased long before the patient feels ill. For example, white blood cells and protein may be present in chronic glomerulonephritis or in other kidney diseases.

What parts of the urinary tract are most frequently infected?

How can bacteria get into the kidneys?

What are the symptoms of urethral infection and bladder infection?

What kinds of drugs are used in treating urinary tract infections?

Why is it important to take all of the prescribed medicine for a urinary-tract infection, even after the symptoms have gone?

How do certain bacterial infections result in glomerulonephritis?

What are the effects of severe kidney impairment?

What is the difference between the cysts in polycystic kidney disease and the cysts in parasitic infections?

Vocabulary:

cyst (SIST)--a liquid-filled sac.

glomerulus (glo-MAIR-yoo-lus)--a ball of coiled capillaries in a nephron.

glomerulonephritis (glo-MAIR-yoo-lo-nuh-FRY-tiss)--a disease affecting the kidneys' capillaries.

kidney stones--stones chat form in the kidney due to precipitation of substances from the urine.

polycystic (PAHL-ee-SIS-tik)--containing many cysts.

pyelonephritis (PY-uh-lo-nuh-FRY-tiss)--a condition resulting from the effects of bacterial infection of the kidneys.

REVIEW SET 23:

1. List at least two important functions of the kidneys.

2. List at least two ways in which the kidneys contribute to homeostasis.

3. a. Where do the circulatory system and urinary tract meet?

   b. What happens at the meeting place?

4. How does active transport contribute to the function of the kidneys?

5. a. List two hormones that are important to the excretory process.

   b. Where is each hormone made?

   c. What are their functions?

6. List at least three things commonly tested for in urinalysis.

7. How are catheters and cystoscopes used in diagnosing or treating kidney disorders?

8. State the basic principle of the "artificial kidney" in terms of diffusion and dialysis.

9. Why is tissue typing required in kidney transplants?

10. a. What is shock?

    b. List at least three conditions that may lead to shock.

11. List the organs urine passes through in the process of excretion.

12. List two paths of entry for bacteria that cause infection of the urinary tract.

13. List and describe at least two kidney disorders.

14. Why is it important to keep taking all of the prescribed medicine for a bacterial urinary-tract infection even after the symptoms have passed?

15. How does the liver assist the kidneys in performing their functions?

UNIT REVIEW SET:

1. List two major functions of blood carried out during circulation.

2. a. Name the five major types of blood vessels.

   b. Which type is the smallest in diameter?

   c. Which type carries blood away from the heart?

d. Which type carries blood toward the heart?

3. a. What happens to the speed of blood as it flows from the arteries through arterioles and then through capillaries?

b. What characteristic of the vessels is largely responsible for this?

4. What is the advantage of blood flowing slowly through capillaries?

5. List two mechanisms which help return venous blood to the heart.

6. Suppose a cell is placed in a solution of higher protein concentration than that of the fluid inside the cell. Is the cell more likely to shrink or swell? Explain.

7. a. What is the name of the process by which oxygen moves out of the blood and into the interstitial fluid?

b. Describe this process in terms of concentration of oxygen.

c. In which organs does oxygen diffuse into the blood?

8. How is the left ventricle of the heart adapted to exert more pressure than the right ventricle?

9. Place the following structures in the sequence in which blood flows through them as it courses through the heart and lungs: pulmonary artery, left atrium, right atrium, aorta, lungs, left ventricle, right ventricle, pulmonary veins, lungs, venae cavae. Begin with the venae cavae.

10. When blood hits an obstruction, a sound is produced. What obstructions play a role in producing the normal heart sounds heard through a stethoscope?

11. What does each number in the following statement stand for? "Patient's blood pressure is 115/85."

12. Explain why blood pressure may drop after a heart attack.

13. Name two mechanisms by which the body can increase the heart rate.

14. In addition to increasing the heart rate, how else is more blood pumped by the heart during exercise?

15. Name a condition that changes the QRS complex.

16. What do the P, QRS, and T waves in an ECG represent?

17. a. True or false: the best way to tell whether atherosclerosis of the coronary arteries is present is with an ECG during rest, rather than during exercise.

b. Explain your answer.

18. State at least three risk factors correlated with myocardial infarction.

19. What are the two major types of blood cells? How do they compare in number, size and shape when viewed with a microscope?

20. a. What chemical substance found in blood is responsible for carrying oxygen?

b. In what part of the blood is this substance found?

c. What disease results from too little of this substance?

21. a. What is meant by a specialized cell?

b. Give at least three examples and state the function of each.

c. What is meant by cellular differentiation?

22. a. What are the three compartments in the body in which water is found?

b. Which compartment contains the most water?

c. Which contains the least water?

23. a. The swelling that comes from a bump on the head is due in part to capillary damage. Explain how. (Hint: Damaged capillaries leak proteins.)

b. What is the swelling called?

24. a. What is blood plasma?

b. What do the five bands seen in the electrophoresis of plasma represent?

25. a. What is the major function of white blood cells?

b. Name two different kinds of white blood cells and the different action of each.

26. a. What are antibodies?

b. How are antibody titers related to immunity?

27. a. What is the major disadvantage of passive immunity compared to active immunity?

b. When is passive immunity used to fight disease?

28. a. What is meant by clotting time?

b. In what disease is it increased?

29. a. What is the relation between pH and acidity?

b. What is the value of the buffers in the blood?

c. Name at least two buffers in the blood.

30. The following is the equation for an acetate buffer at equilibrium. Use this equation to explain why acetate buffer tends to resist a pH change when small amounts of acid or base are added.

$$HC_2H_3O_2 \rightleftharpoons H^+ + C_2H_3O_2^-$$

31. List two ways in which the body acts to maintain or increase the volume of body fluids when you drink too little water.

32. a. What is homeostasis?

b. List at least two characteristics of the blood which the kidneys help to keep within normal limits.

33. Approximately 180 liters of water leave the blood in the kidneys every day.

a. Into which structures in the kidneys does the water go?

b. Explain how active transport helps most of this water to return to the blood.

34. When you eat more salt than usual, the kidneys excrete more salt than usual so the excess salt is removed from the body. List at least one factor that causes the kidneys to respond to the high salt intake in this way.

35. List at least three things commonly tested for in urinalysis, and the diseases that would cause the results to be abnormal.

36. a. List two substances that are removed from the blood by the artificial kidney.

b. Use the concepts of diffusion and dialysis to explain the process.

c. List one substance that the artificial kidney adds to the blood of someone with kidney failure.